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Synthesis of C_2-Tritwistane, Synthetic and Theoretical Studies toward Polytwistane and Syntheses of Twistanamines as Potential Antiviral Agents

von
Martin Olbrich
aus
München, Deutschland

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Erklärung

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Eidesstattliche Versicherung

Diese Dissertation wurde eigenständig und ohne unerlaubte Hilfe erarbeitet.

München, den

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Martin Olbrich

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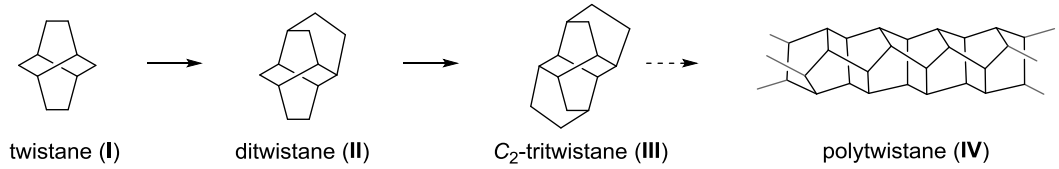
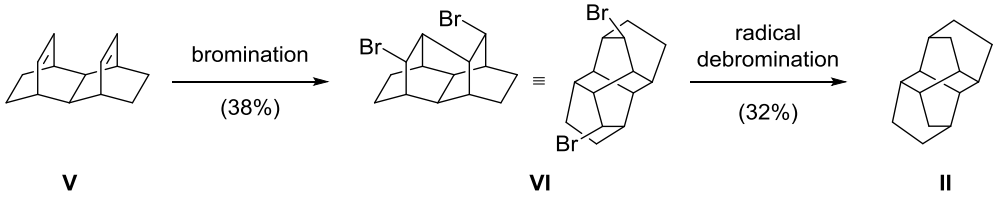
‘On the Route to a Polymer with a Twistane Scaffold’, M. Olbrich, D. Trauner, Vienna International Symposium on Organic Chemistry, Vienna, Austria, 21.05.2011.

ABSTRACT

Discoveries in hydrocarbon chemistry have deeply impacted the development of organic chemistry and still continue to provide important insights for numerous scientific disciplines. The first part of this thesis reviews the recent developments of this field (Chapter 1). One hydrocarbon with especially intriguing structural properties, twistane (**I**), is the focus of this PhD thesis. By theoretical extension of twistane (**I**) with ethano units *via* ditwistane (**II**) and C_2-tritwistane (**III**), maintaining the D_2-symmetric twist-boat conformation, a structurally novel polymer was proposed and termed polytwistane (**IV**).



During the first part of this work, the synthesis of oligotwistanes *via* electrophilic addition reactions to laticyclic conjugated oligoenes such as diene **V** was pursued (Chapter 2). This eventually resulted in the successful synthesis of C_2-tritwistane (**II**), *via* dibromide **VI**, and additionally provided valuable insights into Wagner-Meerwein rearrangements in the bicyclo[2.2.2]octane system. The spectroscopic data obtained from C_2-tritwistane (**II**) might help in the identification of polytwistane (**IV**).



In the next part, possible synthetic strategies for polytwistane (**IV**) were outlined (Chapter 3). For the investigation of an initiator-biased acetylene polymerization, two initiator compounds with different bias to the helicity of polytwistane (**IV**) were synthesized on scale. The crucial step of the polymerization was studied on both systems employing transition metal catalysis as well as radical conditions but did not allow for the synthesis of polytwistane (**IV**) yet. During this work, several novel palladium complexes, including a rare alkenyl palladium complex, were synthesized, isolated and characterized by single crystal X-ray diffraction. To facilitate its synthesis and characterization, the ^{1}H and ^{13}C NMR chemical shifts of polytwistane (**IV**) were elucidated using computational methods.

Work dealing with the search for alternative antiviral agents with activity against mutants of the influenza A virus, which are resistant to classic adamantane derived drugs, such as amantadine, is described in the last part of this thesis (Chapter 4). Potential antiviral agents based on the twistane scaffold were designed for this purpose. Significant progress toward the synthesis of these twistanamines is reported.

ACKNOWLEDGMENTS

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My biggest thank you goes to my wife Sophie and my children Lara and Tom for completing my world, loving me and being always there for me. I love you.

LIST OF ABBREVIATIONS

Å	angstrom
Ac	acetyl
Ad	adamantyl
AIBN	azobisisobutyronitrile
Ar	undefined aryl substituent
ATR	attenuated total reflection (IR)
BAIB	(diacetoxyiodo)benzene
BDE	bond dissociation energy
bipy	2,2'-bipyridin
Bn	benzyl
Bu	butyl
calcd.	calculated
CCDC	Cambridge crystallographic data center
CNT	carbon nanotube
COSY	correlation spectroscopy (NMR)
Cp	cyclopentadienyl
CSA	camphorsulfonic acid
CyJohnPhos	(2-biphenyl)dicyclohexyl-phosphine
d	day(s)
d	dublet (NMR)
d	deuteron
δ	chemical shift (NMR)
DDQ	2,3-Dichloro-5,6-dicyano-1,4-benzoquinone
DIBAL-H	diisobutylaluminum hydride
DIPA	diisopropylamine
DMAP	4-(dimethylamino)pyridine
DMF	dimethylformamide
DMP	Dess-Martin-periodinane
DMPU	*N*,*N*'-dimethylpropyleneurea
DMSO	dimethyl sulfoxide
dppp	1,3-bis(diphenylphosphino)-propane
DW	double-walled
E	opposite (*trans*)
EI	electron ionization (MS)
eq.	equivalent(s)
ESI	electrospray ionization (MS)
Et	ethyl
expm.	experimental
FGI	functional group inter-conversion
FVP	flash vacuum pyrolysis
g	gram(s)
GC	gas chromatography
h	hour(s)
Hal	undefined halogen atom
HMBC	heteronuclear multiple-bond correlation spectroscopy
HMDS	hexamethyldisilazane
HMPA	hexamethylphosphoramide
HPLC	high pressure liquid chromatography
HRMS	high resolution mass spectrometry
HSQC	heteronuclear single-quantum correlation spectroscopy
Hz	Hertz
i	iso (isomer)
imid.	imidazole
IR	infrared
IUPAC	International Union of Pure and Applied Chemistry
J	coupling constant (NMR)
k	kilo (10^3)
L	liter

LDA	lithium diisopropylamide
m	multiplet (NMR)
m	milli (10^{-3})
m	meta
M	molar
m-CPBA	*m*-chloroperoxybenzoic acid
Me	methyl
Mes	mesitylene
min	minute(s)
mol	mole(s)
mp	melting point
MS	mass spectrometry, molecular sieves
Ms	methanesulfonyl
n	normal (isomer)
NBS	*N*-bromosuccinimide
NIS	*N*-iodosuccinimide
NMO	*N*-methylmorpholine *N*-oxide
NMR	nuclear magnetic resonance
NOESY	nuclear Overhauser effect spectroscopy
o	ortho
p	para
p	pressure
PCC	pyridinium chlorochromate
Ph	phenyl
PPA	polyphosphoric acid
ppm	parts per million (NMR)
pyr	pyridine
q	quartet
R	undefined substituent
R_f	retention factor
rt	room temperature
s	singlet
t	tertiary (isomer)
t	triplet
TBAF	tetra-*n*-butylammonium fluoride
TBS	*tert*-butyldimethylsilyl
TES	triethylsilyl
Tf	trifluoromethanesulfonyl
TFA	trifluoroacetic acid
THF	tetrahydrofuran
TIPS	tri-*iso*-propylsilyl
TLC	thin layer chromatography
TMEDA	tetramethylethylenediamine
TMS	trimethylsilyl
TMP	2,2,6,6-tetramethylpiperidine
Tol	*p*-tolyl
TPAP	tetra-*n*-propylammonium perruthenate
Trt	triphenylmethyl
Ts	toluenesulfonyl
W	watt(s)
wt%	mass percentage
Z	together (*cis*)

TABLE OF CONTENTS

THEORETICAL PART

1 Introduction

1.1 Modern Hydrocarbon Chemistry

A hydrocarbon is, as the name already states, a binary compound made up from carbon and hydrogen atoms. Despite being composed of only three basic building blocks (Figure 1), hydrocarbons are a vast class of compounds with uncountable members.[1]

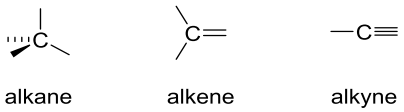


Figure 1. Building blocks in hydrocarbon chemistry (adopted from Hopf[1]).

This variety is due to the ability of carbon atoms to catenate, meaning to form branched and linear compounds by bonds between atoms of the same element. The determining factor for this property is the bonding energy of the carbon atoms among each other. One essential gauge for the strength of a chemical bond is the bond dissociation energy. The small choice of values in Table 1 shows that carbon-carbon bonds are generally quite strong if one considers labile bonds like I─I and very strong bonds like C_{alkyl}─F as a reference.[2] The bond strength and thereby catenation ability of the element carbon, together with steric and electronic effects, such as the similar electronegativity of the element hydrogen, accounts for the richness of the compound class.

Table 1. Bond dissociation energies in the building blocks of hydrocarbon chemistry.

Bond	BDE [kcal·mol^{-1}]	Bond	BDE [kcal·mol^{-1}]
$C_{benzyl/allyl}$-H	90	C_{alkyl}-C_{alkyl}	90
C_{alkyl}-H	100	$C_{vinyl/arene}$-C_{alkyl}	100
H-H	105	$C_{acetylene}$-C_{alkyl}	125
$C_{vinyl/arene}$-H	110	C_{vinyl}-C_{vinyl}	160
$C_{acetylene}$-H	133	$C_{acetylene}$-$C_{acetylene}$	200
C_{alkyl}-F	115	C_{alkyl}-I	56
O=O	119	I-I	36

Owing to this huge diversity, hydrocarbon compounds are divided in the classifications alkanes, alkenes, alkynes and arenes according to their composition regarding the building blocks of hydrocarbon chemistry (Figure 1). Another defining feature which bears relation to this classification is the degree of saturation, also termed index of hydrogen deficiency, which is again directly linked to the H:C ratio. The highest possible H:C ratio for a stable hydrocarbon compound is 4.0, limited by the four valence electrons of the element carbon, and can be found only in methane. Naturally, hydrocarbons are found most notably in natural gas and crude oil, but are also ubiquitous in outer space displaying interesting phenomena like the liquid hydrocarbon lakes on Titan, which is Saturn's

largest moon.[3] Hydrocarbons from natural sources display H:C ratios from 3.8 in natural gas, which consists mainly of methane, to 0.2 in bituminous coal and anthracite, which contain mostly polyaromatics.[4] In classic compounds of hydrocarbon chemistry the H:C ratio ranges from ~2, like in tetrahedrane **1**, with increasing degree of unsaturation as displayed in structures **2**, **4**, **6**, **7** and **8**, and an increase in the number of rings like in **3**, **5**, **7** and **8**, to values as low as 0.03 in fullerene hydride **8** (Figure 2).

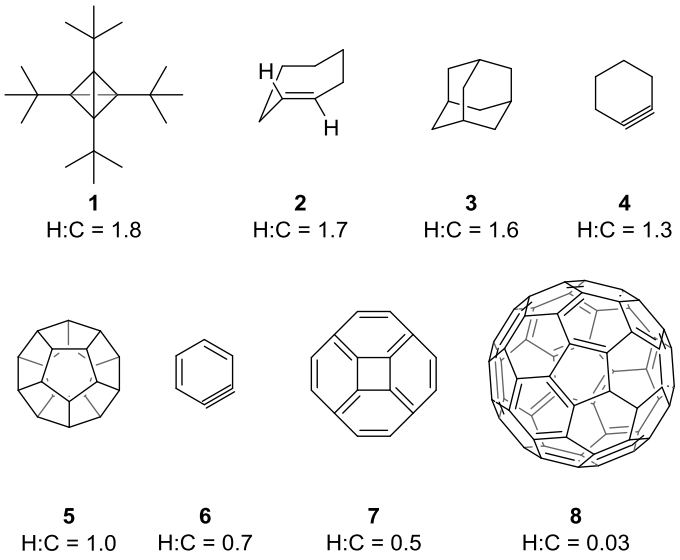


Figure 2. H:C ratio of a selection of some classic hydrocarbons.

Because of their chemical and physical characteristics, as well as their natural abundance, hydrocarbons from fossil fuels became the world's primary energy source. Also, despite all current attempts to shift to renewable resources, this situation will not change in the foreseeable future. Furthermore, hydrocarbons can be viewed as the foundation of organic chemistry. Not only are petrochemicals, hydrocarbons derived by cracking and reforming from petroleum, the feedstock of the chemical industry. The contributions to the comprehension of chemical reactivity and structure made by studying hydrocarbons and their reactions are manifold. In modern hydrocarbon chemistry this is continued in studying unusually bonded and strained compounds. This includes for example the planarization of sp^3 hybridized carbon centers, the distortion of double and triple bonds as well as the deformation of aromatic systems (Figure 3).

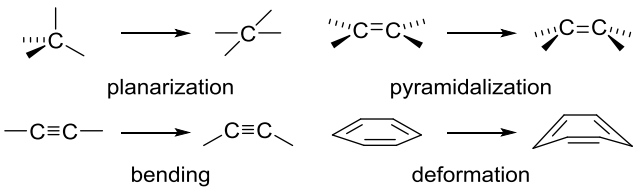


Figure 3. Topics of investigation in modern hydrocarbon chemistry (adopted from Hopf[1]).

In addition to this fundamental research, new structures, especially polymeric ones, are developed aiming at applications in everyday life. In the following section, a short overview of the development of hydrocarbon chemistry mainly from 2000 to 2014 is given, structured loosely according to the seminal book by Hopf on *Classics in Hydrocarbon Chemistry*.[1]

1.2 Alkanes

For an account of hydrocarbon chemistry, starting with the platonic hydrocarbons could not be more fitting, as the platonic hydrocarbons arguably are considered the most classic compounds in hydrocarbon chemistry. The three possible hydrocarbon compounds corresponding to the platonic solids (Figure 4), tetrahedrane (**9**), cubane (**10**) and dodecahedrane (**5**) attracted interest more than 50 years ago due to their symmetric structures and the synthetic challenge in surmounting the strain and the curvature of the molecules. Although dodecahedrane (**5**) was seen by some as "the Mount Everest of hydrocarbon chemistry",[5] the completion of its synthesis in 1982[6] did not diminish interest in the field. If anything it sparked new work on the chemistry of dodecahedrane (**5**) and new efforts to synthesize tetrahedrane (**9**).

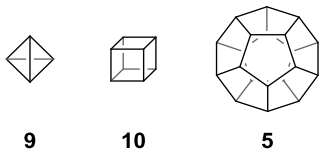
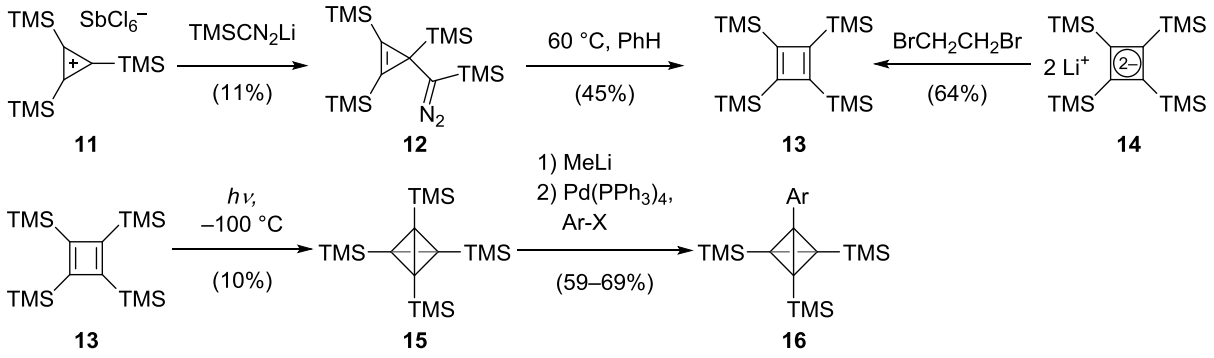


Figure 4. The platonic hydrocarbons.

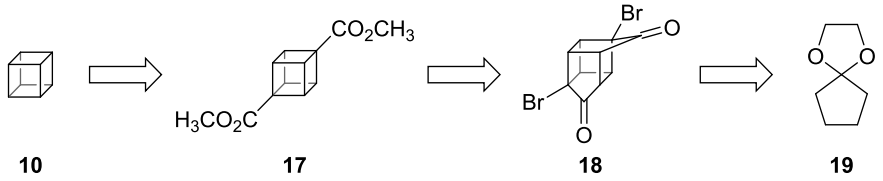
As of today, tetrahedrane (**9**) is still an experimentally unrealized entity of hydrocarbon chemistry, although Schreiner *et al.* showed with exhaustive calculations that **9** is a kinetically stable and synthesizable compound.[7] After the first synthesis of a tetrahedrane derivative, tetra-*tert*-butyltetrahedrane (**1**), in 1978 by the group of Maier[8] the continuing quest for the parent hydrocarbon led to a few other reports of tetrahedrane derivatives but the parent hydrocarbon remained elusive.[9] In 2001 the groups of Maier and Sekiguchi reported the synthesis of novel tetrakis(trimethylsilyl)tetrahedrane (**15**) *via* photoisomerization of cyclobutadiene **13**, which was synthesized by two independent methods (Scheme 1).[10] In Maier's synthesis, cyclopropylcation **11** was converted to diazocompound **12**, which expels nitrogen upon heating in benzene and forms, after C-C bond insertion of the resulting carbene, the ring expanded product **13**.[11] Sekiguchi's synthesis was based on the oxidation of aromatic dianion **14**, which allowed for access to **13** on a half-gram-scale.[12] Photoisomerization of cyclobutadiene **13** provided the desired tetrahedrane **15**, albeit in low yield. The isomerization step was later substantially improved to 50% yield by the group of Sekiguchi using one-electron oxidation conditions, allowing the synthesis on gram-scale.[13] Characterization of tetrahedrane **15** showed it to be unexpectedly stable and provided the first X-ray structure of a tetrahedrane without disorder. Above all, it was found by the group of Sekiguchi that lithiation[14] of

15 enabled the cross-coupling of the tetrahedrane cage to arenes.[15] Thereby a variety of functionalized tetrahedranes **16** was accessed.



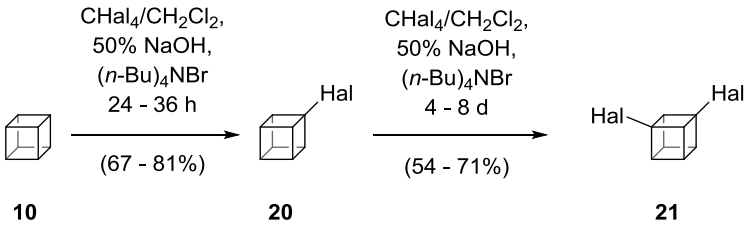
Scheme 1. Synthesis of $(TMS)_4$-cyclobutadiene (**13**) and isomerization to $(TMS)_4$-tetrahedrane (**15**).[10]

In contrast, cubane (**10**) was already synthesized in 1964 by the group of Eaton.[16] Owing to continued interest in the structure of cubane (**10**) for example as a rigid scaffold in pharmaceuticals, a pilot-scale synthesis of cubanedicarboxylate **17** was reported recently (Scheme 2).[17] The synthesis proceeds in eight steps from commercially available cyclopentanone ketal **19** and gives cubanedicarboxylate **17** in 22% overall yield, notably employing a photocyclization on 8.5 mol-scale.



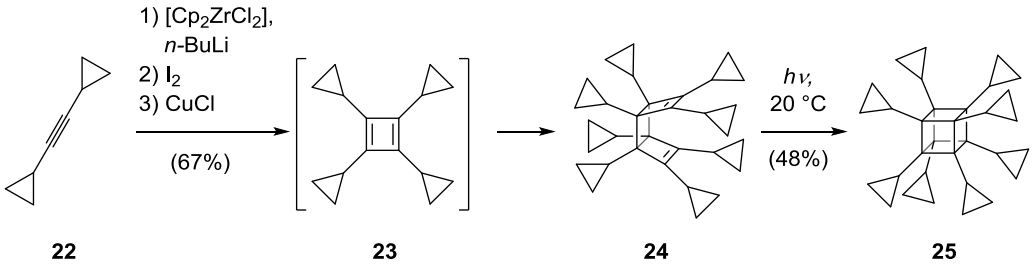
Scheme 2. Retrosynthetic analysis of cubane (**10**).[17]

As a consequence of the established synthesis of cubane (**10**), a multitude of cubane derivatives exist. Some of these, such as dicarboxylate **17**, originate from intermediates of the cubane synthesis.[18] Additionally, selective functionalization of cubane (**10**) was developed by the group of Schreiner, thereby broadening the scope of available cubane derivatives (Scheme 3).[19] Using mild phase-transfer conditions monohalogenated cubanes **20** were obtained in good yields, which could be further reacted to homo- and heterodihalogenated cubanes **21**.



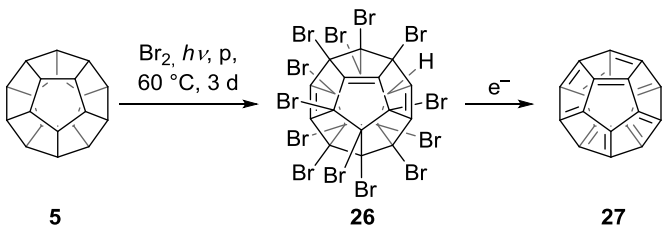
Scheme 3. Selective mono- and dihalogenation of cubane (**10**) using phase-transfer conditions.[19]

In 2007 de Meijere *et al.* reported the synthesis of the remarkable octacyclopropylcubane (**25**) (Scheme 4).[20] In their synthesis they employed a method reported by Takashi *et al.*[21] for the transformation of dicyclopropylacetylene (**22**) into cyclobutadiene **23**, which dimerized immediately to tricycle **24** in a Diels-Alder reaction. Irradiation of this material afforded cubane **25** in a moderate yield of 48%. Despite the immense strain energy in the structure of cubane **25**, this derivative is kinetically stabilized compared to cubane (**10**), exhibiting a half-life of 3 h at 250 °C. Analysis by single crystal X-ray diffraction showed C_{4h}-symmetry for the molecule in the solid state.



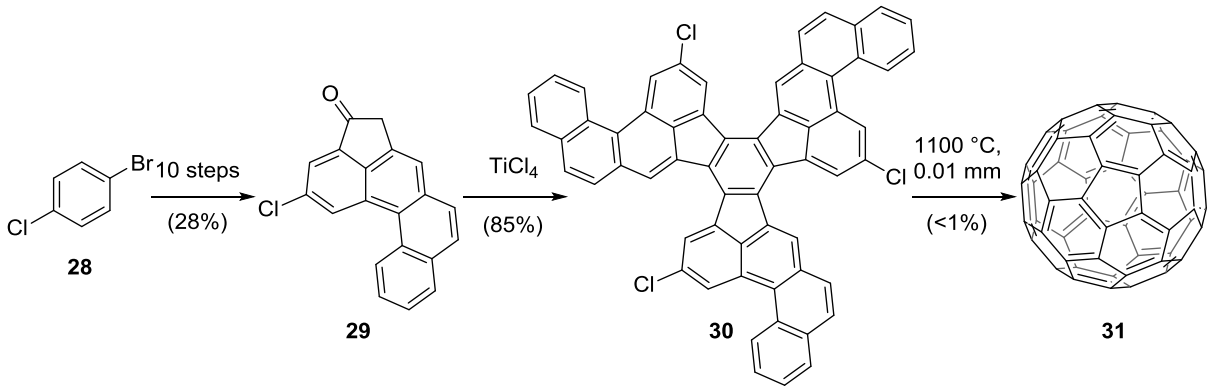
Scheme 4. Synthesis of octacyclopropylcubane (**25**) by de Meijere.[20]

As already mentioned, dodecahedrane (**5**) succumbed to synthesis in 1982.[6] Some years later a second route to **5** was developed by the group of Prinzbach.[22] This group also worked extensively on the functionalization of dodecahedrane (**5**),[23] which in 2000 ultimately led, *via* perbrominated intermediate **26**, to the synthesis of the smallest possible fullerene C_{20} (**27**) which had a very short lifetime (≥0.4 ms) and was only detectable by mass spectrometric methods (Scheme 5).[24]



Scheme 5. Perbromination of **5** and subsequent synthesis of fullerene C_{20} (**27**) by gas-phase debromination.[24]

Regarding fullerenes, shortly after the synthesis of C_{20} (**27**) a rational total synthesis of buckminsterfullerene (**31**) was reported in 2002.[25] The synthesis relied on the assembly of the carbon framework by a trimerizing aldol condensation of **29**, which was accessed in a 10 step synthesis from 1-bromo-4-chlorobenzene (**28**) employing standard chemistry (Scheme 6). C_{60} (**31**) was then obtained by flash vacuum pyrolysis (FVP) of precursor **30** in very low yield, thereby demonstrating the power of directed cyclodehydrogenation reactions for the synthesis of geodesic polyarenes.



Scheme 6. Rational total synthesis of buckminsterfullerene (**31**).[25]

In their work on dodecahedrane (**5**), Eaton and Müller first described the family of peristylanes and synthesized the first member, [5]peristylane (**36**).[26] Later, Garratt and White generalized the concept of peristylanes as compounds "in which an *n*-membered ring is joined by alternate carbon atoms to a 2*n*-membered ring".[27] They also proposed the corresponding structures where a second *n*-membered ring closes the spherical shape. In this way [3]peristylane (**32**) leads to D_{3d}-octahedrane (**33**), [4]peristylane (**34**) belongs to D_{4d}-decahedrane (**35**), [5]peristylane (**36**) to dodecahedrane (**5**) and [6]peristylane (**37**) to C_{24}-fullerane (**38**) (Figure 5).

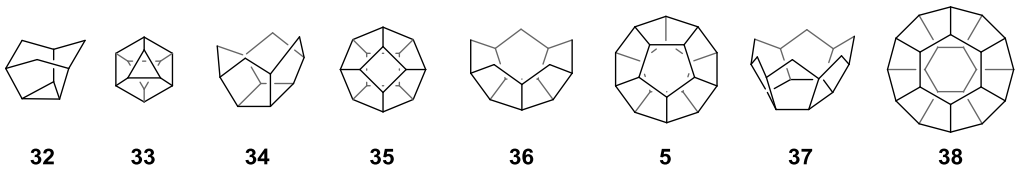
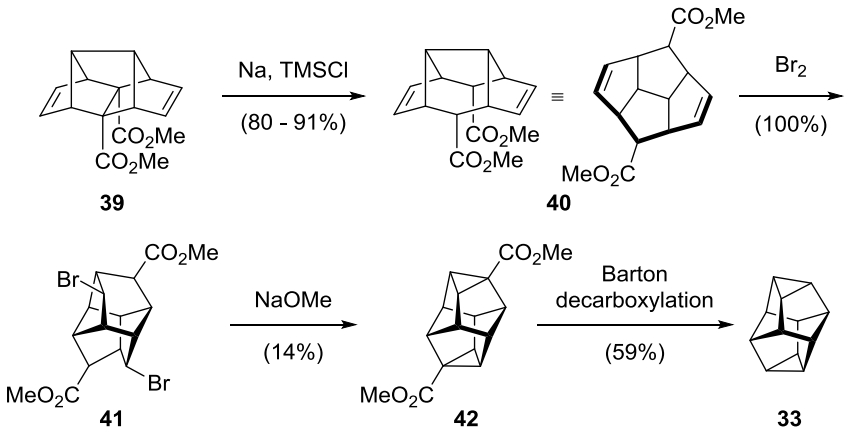


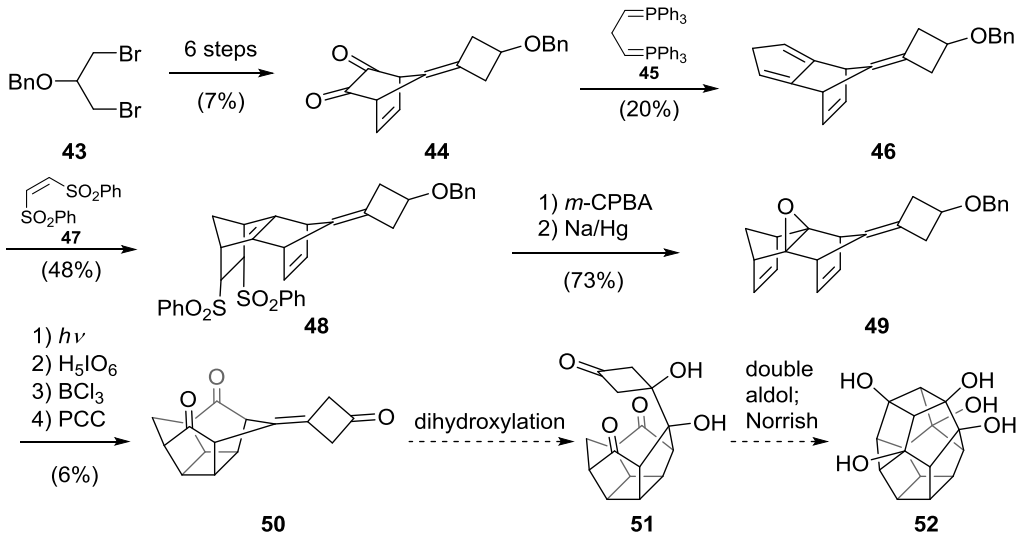
Figure 5. Peristylanes and the corresponding closed structures.

The group of de Meijere accomplished the first synthesis of D_{3d}-octahedrane (**33**), starting from compound **39**, which is renowned from Paquette's dodecahedrane (**5**) synthesis (Scheme 7).[28] Reductive cleavage of the central C-C bond afforded diester **40**. This was transformed in an N-type cyclization of the laticyclic homoconjugated double bonds into **41**, thereby closing the six-membered ring of octahedrane **33**. Under alkylation conditions the cyclopropane moieties were accessed, giving the desired octahedrane carbon skeleton in **42**. Finally, decarboxylation using Barton's radical procedure afforded the parent hydrocarbon **33**. In further studies it was shown that octahedrane **33** is the most stable $(CH)_{12}$ hydrocarbon, despite containing more strain energy per C─C bond than decahedrane **35** and dodecahedrane (**5**).[29] Using the phase-transfer catalytic halogenation conditions developed by the group of Schreiner, octahedrane **33** was also functionalized as shown for the similarly strained cubane system (Scheme 3).



Scheme 7. Synthesis of D_{3d}-octahedrane (**33**) employing a cyclization of homoconjugated double bonds.[28]

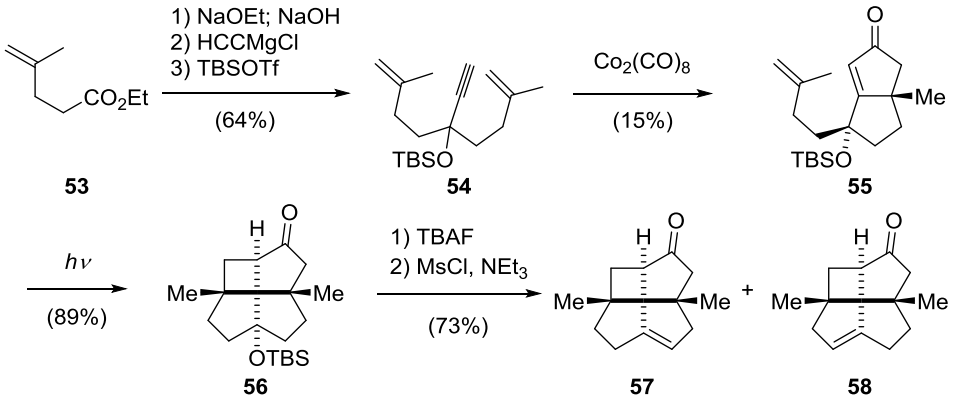
Prompted by the synthesis of **33**, Shen and Paquette reported their efforts toward the synthesis of decahedrane **35**, which ultimately yielded [4]peristylane **50** (Scheme 8).[30] Conversion of dibromide **43** to **44** was accomplished in six steps, followed by a double Wittig reaction with ylid **45** to generate the cyclopentadiene moiety in **46**. Subsequently the last two carbon atoms required for the carbon skeleton of **33** were introduced using ethylene equivalent **47** in a Diels-Alder reaction affording **48**. Epoxidation and liberation of the masked double bond gave diene **49**. Photocyclization followed by cleavage of the epoxide to the diketone afforded the [4]peristylane carbon framework, which upon deprotection and oxidation resulted in precursor **50**. The further synthetic strategy was to bend the cyclobutane moiety over the peristylane by a dihydroxylation and close the spherical molecule using several aldol reactions. However, to date the completion of the decahedrane cage has not been achieved.



Scheme 8. Synthesis of [4]peristylane **50** as a synthetic precursor for decahedrane **35**.[30]

So far only spherical $(CH)_n$ structures, which are of interest mainly for their symmetry, molecular curvature and for the strain energy exhibited in these systems, were contemplated in this text. As

pointed out in section 1.1, interest in hydrocarbon chemistry is focused mainly on carbon atoms in unusual and strained environments. One research topic along these lines is the flattening of sp^3 hybridized carbon centers. The compound family which is the most prominent for this purpose is named fenestranes and is made up from four fused carbocycles which all share one central carbon atom. Although the first synthesis of a fenestrane dates back more than 40 years,[31] new efforts toward even more flattened systems were reported recently by the group of Keese (Scheme 9).[32] For establishing the fenestrane system a synthetic sequence of a Pauson-Khand reaction and a photocyclization were used in this synthesis. The precursor **54** was synthesized from **53** by a sequence of Claisen condensation, decarboxylation, alkyne addition and silyl protection. An ensuing Pauson-Khand reaction proceeded as planned, albeit in low yield, to afford cyclopentenone **55**, which was cyclized photochemically to fenestrane **56**. This compound was characterized by single crystal X-ray diffraction and displayed angles about the central carbon atom of 128.9° and 122.8°, deviating substantially from the tetrahedral angle. To increase the flattening effect, a bridgehead double bond was introduced by deprotection and mesylation resulting in isomers **57** and **58**. Unfortunately no determination of the angles about the central carbon were reported for these fenestrenones and similar studies in an even more interesting system failed to give the desired products, resulting only in fragmentation of the fenestrane skeleton due to the immense strain energies.



Scheme 9. Synthesis of fenestranes **57** and **58** with incorporation of bridgehead double bonds in order to increase the flattening of the central carbon atom.[32]

Another example for an unusual chemical environment is the cyclohexane ring in the boat conformation, which is about 6 kcal·mol^{-1} higher in energy than the corresponding chair conformation.[33] For this reason the boat conformation has to be locked by chemical bonds to persist in a molecule. In hydrocarbon chemistry the compound classes of barrelanes and asteranes meet this requirement (Figure 6). The barrelanes implement the conformational lock by the bicyclo[2.2.2]octane cage, like in barrelene (**59**). Whereas in the asteranes the lock results from the link of two *n*-membered rings by *n* methylene bridges, as in the experimentally yet unrealized pentaasterane (**60**). During their work on atropurpuran (**61**)[34] Suzuki *et al*. developed a synthetic route to dibarrelanes resulting in the

synthesis of the parent hydrocarbon **70**.[35] On these grounds they proposed new polycyclic compounds resulting from fused barrelanes like cyclopentabarrelane (**62**).

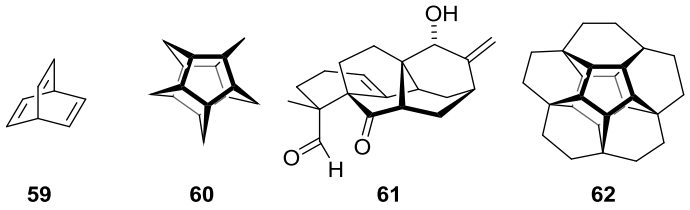
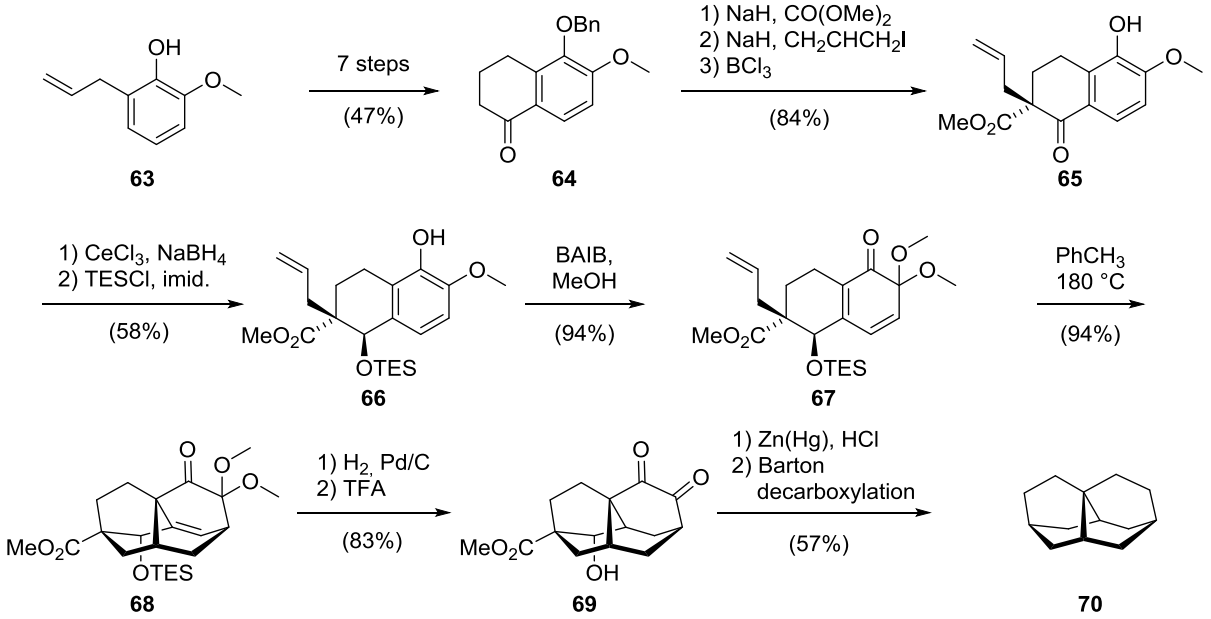


Figure 6. Selected structures of molecules containing cyclohexane rings in the boat conformation.

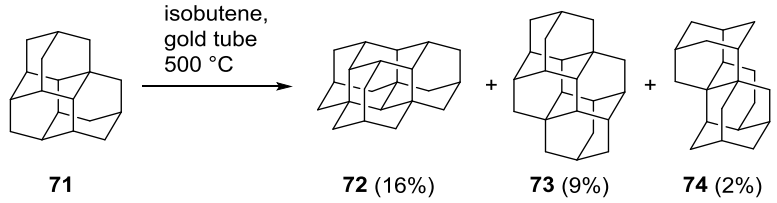
The synthesis of dibarrelane (**70**) commenced with conversion of phenol **63** to tetralone **64** in seven steps (Scheme 10). This material was converted to **65** by subsequent methoxycarbonylation and alkylation, followed by deprotection of the benzylether. After Luche reduction and TES-protection of the thus formed secondary alcohol phenol **66** was obtained. After a hypervalent iodine oxidation to orthoquinone monoacetal **67**, the stage was set for the ensuing reverse electron-demand Diels-Alder reaction which gave dibarrelane **68** in excellent yield. Reduction of the double bond and deprotection afforded **69**. Defunctionalization by way of Clemmensen reduction and Barton decarboxylation finally yielded the parent hydrocarbon **70**. Single crystal X-ray diffraction studies suggested that dibarrelane displays C_2-symmetry instead of the expected C_{2v}-symmetry in the solid state due to distortion of the molecule.



Scheme 10. Synthesis of dibarrelane (**70**) using a reverse electron-demand Diels-Alder reaction.[35]

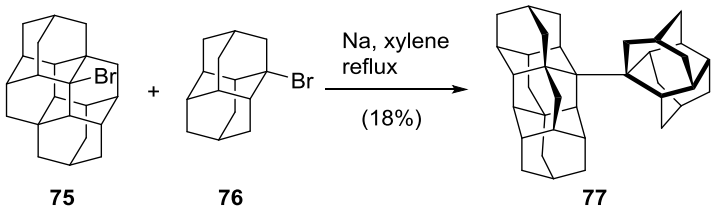
In contrast to the previously mentioned strained compounds are the molecules of the diamondoid series. In this area the scientific interest arises from the extraordinarily high thermodynamic stability of these structures, containing only cyclohexane rings in the chair conformation. Therefore, this field is highly developed and extensively reviewed.[36] The isolation of higher diamondoids from

petroleum[37] led to their availability in research and fueled the work on this topic even more. As a result Dahl *et al*. succeeded in synthesizing higher diamondoids (Scheme 11).[38] In experiments mimicking cracking of petroleum under an atmosphere of isobutene tetramantanes **72**, **73** and **74**, among higher adamantoids, were obtained in fair yields from triamantane (**71**). The results indicated that diamondoids grow by free radical pathways instead of superacid-catalysis, as was assumed earlier. Furthermore, the authors showed that higher diamondoids could be used to grow CVD diamond, which could give the opportunity to access nanodiamonds of defined size.



Scheme 11. Synthesis of higher diamondoids from triamantane (**71**).[38]

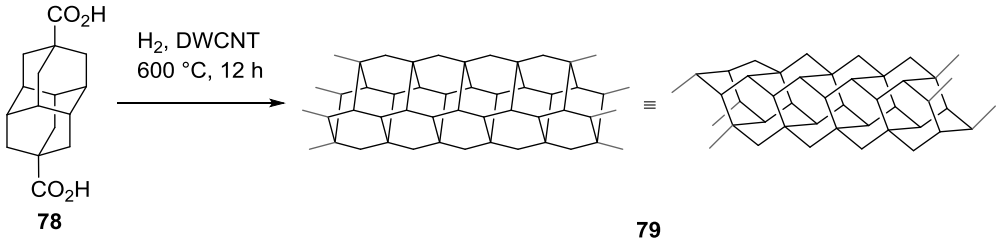
As a consequence of the availability of diamondoids, the functionalization of higher adamantanes is now well established.[36] For this reason, adamantanes were used as sterically demanding scaffolds to probe the boundaries of possible bond lengths. In coupling experiments of higher adamantanes, Schreiner *et al*. managed to synthesize dimers with exceptionally long alkane C─C bonds.[39] In one particular example (Scheme 12), Wurtz coupling of tetramantane **75** with diamantane **76** afforded **77** which displayed a C─C bond length of 1.71 Å, for the bond connecting the adamantane systems, the longest alkane C─C bond to date.[40] The hydrocarbon showed a high thermal stability that defied the common empirical correlation of bond length and bond strength. Utilizing computational chemistry it was shown that steric crowding is not only responsible for bond lengthening but also for the stability of the molecules by attractive dispersion forces between the surfaces of the cages. This could also explain the stabilizing effect of *tert*-butyl groups on strained systems, termed the 'corset effect'.[41]



Scheme 12. Synthesis of an adamantane dimer with a very long C─C bond.[40]

As it was shown that higher adamantanes and even nanodiamonds could be grown from lower adamantanes (Scheme 11), the question arose if it was possible to synthesize one dimensional diamond. Recently, Zhang *et al*. found evidence for the formation of a hydrocarbon nanowire in annealing experiments of diamantane dicarboxylic acid **78** inside of a DWCNT (Scheme 13).[42] IR and Raman analysis of the produced material as well as calculations suggested the formation of a sp^3

nanowire for which the structure of one dimensional nanodiamond **79** would be a reasonable assumption.



Scheme 13. Synthesis of a diamond nanowire **79** from annealing of a diamantane derivative.[42]

Polymeric structures like the diamond nanowires **79** are of particular interest for future applications as similar structures like diamond itself are used industrially.[43] For this reason several polymeric hydrocarbon structures were proposed in recent studies (Figure 7). Minyaev *et al*. theoretically investigated polyprismane structures such as **80**, **81** and **82** and showed their thermodynamic stability.[44] These structures are especially intriguing because of the inverted, pyramidal configuration of the contained carbon atoms. The group of Crespi suggested novel hydrocarbon nanowires which promise high stiffness, high stability and insulating properties.[45] The suggested structures consist of cyclohexane rings in chair and boat conformations in **83** or exclusively in the boat conformation as in **84**. The polymer **85**, built up only of cyclohexane rings in the twist-boat conformation, was proposed by Barua *et al*. and was named polytwistane.[46] This polymer displays helical chirality due to the D_2-symmetry of the constituting twist-boat cyclohexane rings and was also shown to be thermodynamically stable. All of these structures have not yet been realized experimentally but the example of graphane **86** illustrates that a theoretical compound can rapidly become reality. From the first mention of the structure of graphane **86** in the literature in 2003[47] over the prediction of its stability and some properties in 2007[48] to the experimental realization in 2009[49] it took only six years. The success of this project shows that it is worthwhile to pursue also ambitious aims in hydrocarbon chemistry.

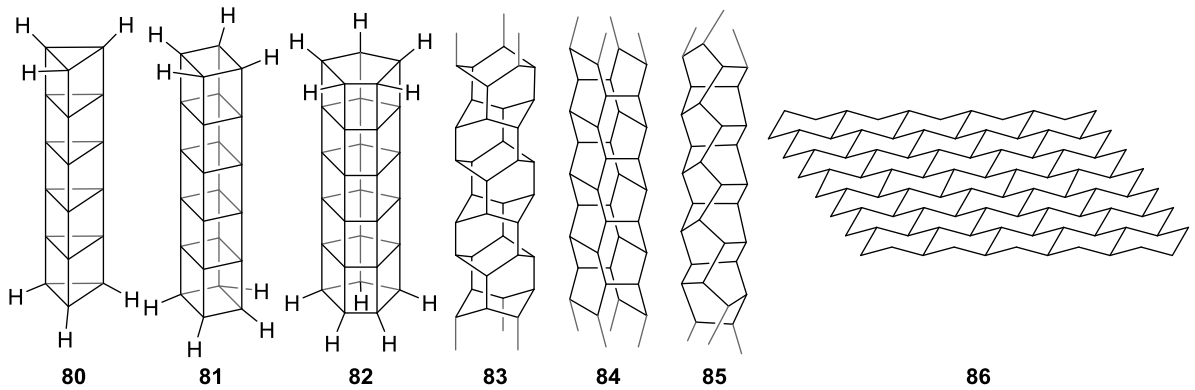
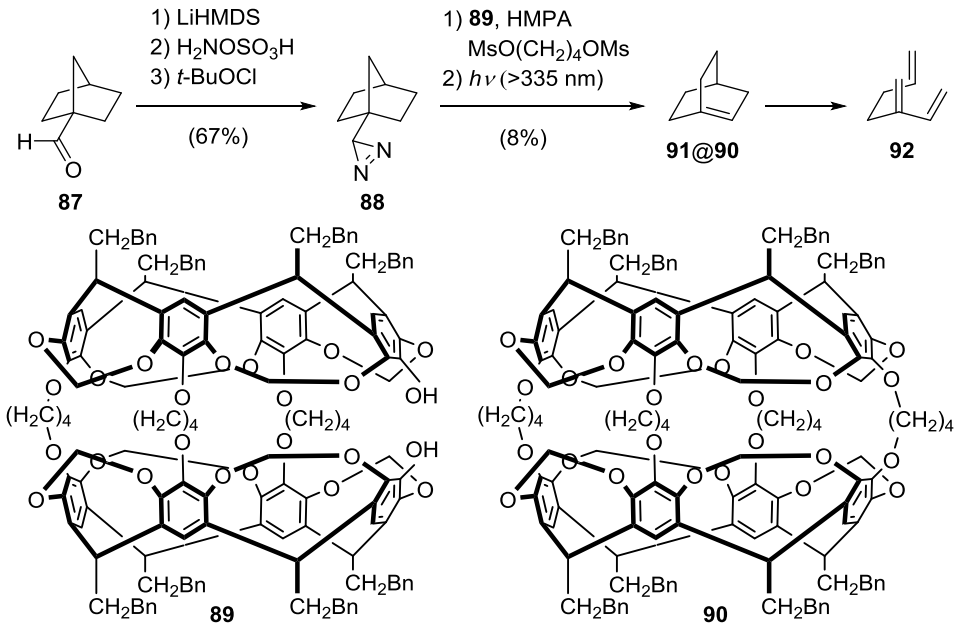


Figure 7. Polycarbocyclic cage structures.[44],[45],[46],[47]

1.3 Alkenes and Alkynes

So far only saturated hydrocarbons have been discussed, thereby covering only structures consisting of one of the three basic building blocks of hydrocarbon chemistry (Figure 1). In this section compounds are considered that contain also the missing two building blocks resulting in alkenes and alkynes.

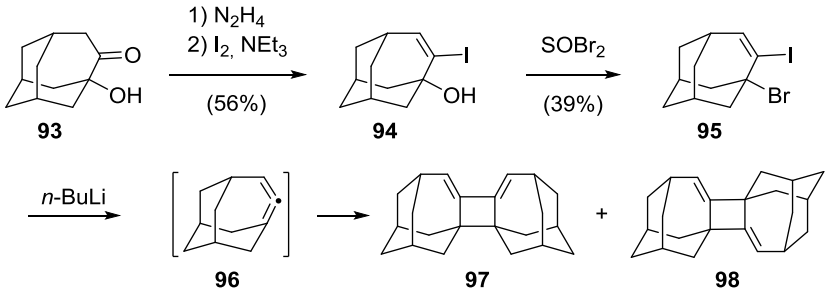
One class of compounds that is historically associated with strain, from the time on when Bredt formulated the rule that double bonds avoid bridgehead positions,[50] is the class of *anti*-Bredt compounds (see Scheme 14 compound **91** for an example of an *anti*-Bredt compound). The strain in these molecules results from the presence of a *trans*-cycloalkene which is a consequence of the bridgehead double bond, which belongs to two carbocycles. Roach and Warmuth reported in 2003 the stabilization of the highly strained *anti*-Bredt compound bicyclo[2.2.2]oct-1-ene (**91**) at room temperature using a host molecule.[51] For the synthesis of bicyclo[2.2.2]oct-1-ene (**91**) a method was employed which was previously used to demonstrate its transient existence.[52] Thus, bridgehead aldehyde **87** was converted to diazirine **88** in a three step protocol (Scheme 14). Diazirine **88** was subsequently incorporated into host molecule **90**, which is a modified version of the container that was used for the room temperature characterization of cyclobutadiene.[53] Irradiation of complex **88**@**90** at specific wavelengths of light gave the complex of bicyclo[2.2.2]oct-1-ene **91**@**90**. Despite the presence of a *trans*-cyclohexene, compound **91**@**90** was stable at 60 °C for longer than one day in the absence of oxygen. This demonstrates that incarceration of compound **91** prevents the major decomposition pathway of a retro-Diels-Alder to **92**, thereby enabling the characterization of **91**.



Scheme 14. Room temperature stabilization of *anti*-Bredt compound **91** by incarceration in **90**.[51]

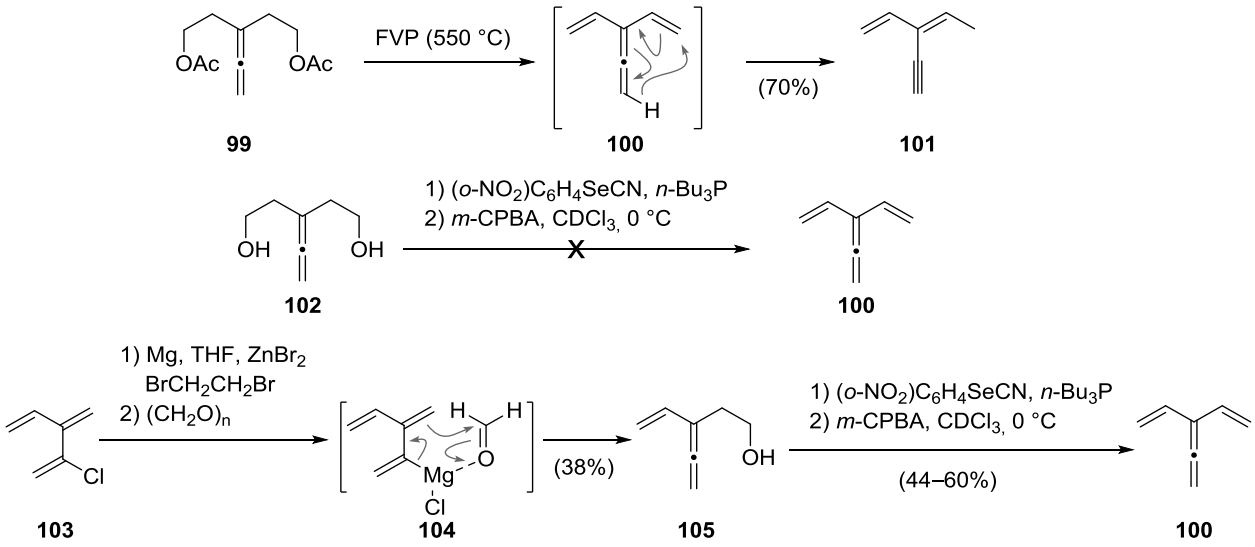
In a related study, Ogawa *et al*. investigated *anti*-Bredt allenes, the combination of a cyclic allene and an *anti*-Bredt compound (Scheme 15).[54] Starting from ketoalcohol **93**, hydrazone formation and iodination afforded alkenyl iodide **94**. This was converted in a bromination reaction to vicinal

dihalide **95**. Upon exposure to *n*-BuLi, metalation and elimination afforded transiently bridgehead allene **96**. This species, containing a 7 membered *trans*-cycloallene, directly dimerized to give dienes **97** and **98**, which are stable *anti*-Bredt compounds as they contain a *trans*-cyclononene.



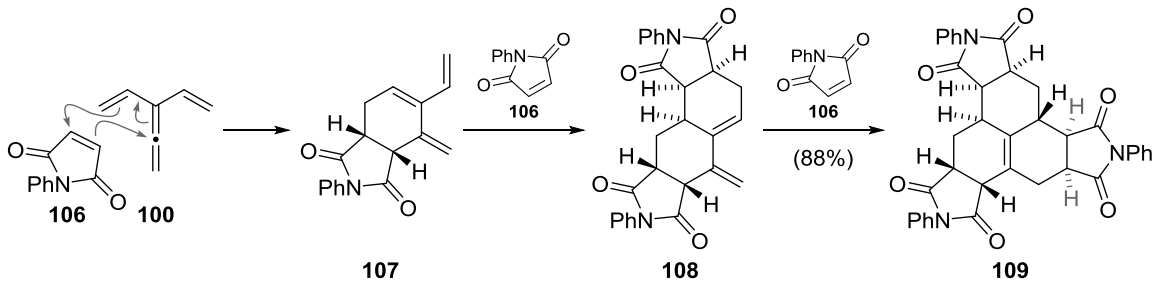
Scheme 15. Intermediate generation of an *anti*-Bredt allene by dehalogenation.[54]

Likewise to all saturated hydrocarbons (section 1.2), all unsaturated hydrocarbon compounds are, of course, possible scaffolds. One compound which contains one of the highest degrees of desaturation relative to the number of carbon atoms it is constituted of without being aromatic is 1,1-divinylallene (**100**) (Scheme 16). This long sought after allene was first transiently observed by Lehrich and Hopf in the FVP of diacetoxyallene **99**.[55] The alkyne **101** resulting from this reaction was reasoned to be the product of a [1,5]-hydride shift of the desired allene **100** which, not surprisingly, was unstable under the FVP reaction conditions. Another route to divinylallene (**100**) by the same group employing a double Grieco elimination of diol **102** also proved unsuccessful.[56] In 2011 the group of Sherburn succeeded in the synthesis of divinylallene (**100**) from triene **103**.[57] Formation of the Grignard reagent and vinylogous formylation *via* **104** provided allene alcohol **105**. Remarkably, elimination of the primary alcohol was carried out also using Grieco's conditions to result in the desired **100**. Compound **100** was found to be reasonably stable if handled in solution and was fully characterized.



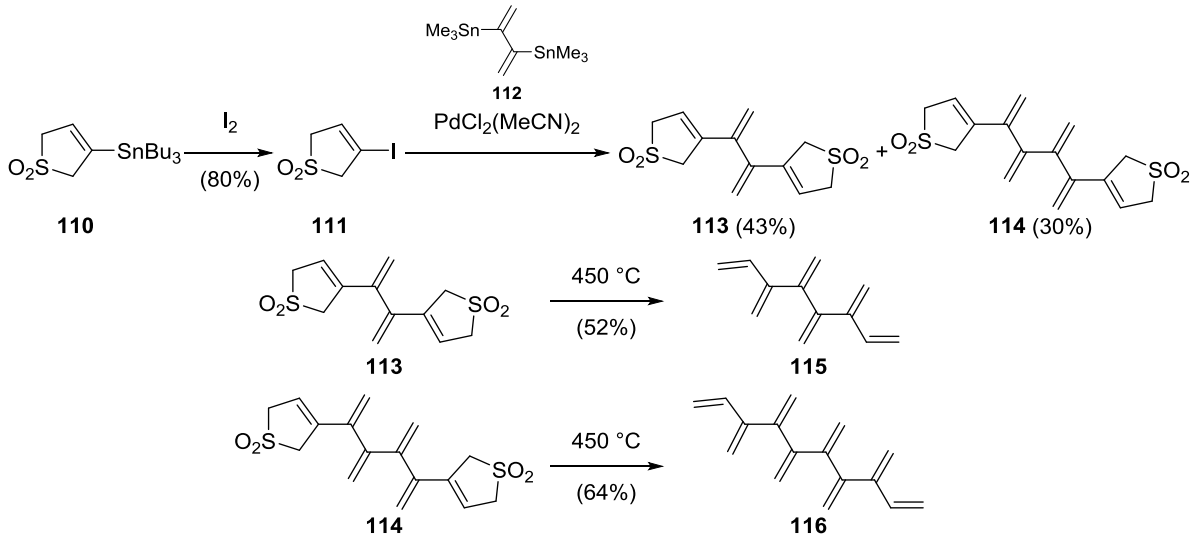
Scheme 16. Futile approaches to divinylallene **100** and the successful synthesis by the group of Sherburn.[57]

Additionally, the reactivity of divinylallene **100** was examined and showed high selectivity in a diene-transmissive Diels-Alder reaction with maleimide **106** (Scheme 17). Only in the last reaction of the Diels-Alder sequence was a mixture of diastereomers obtained, leading to a ratio of 65:35 of isomers at the marked carbon centers in **109**. With the additional possibility to interrupt the sequence after one addition at **107** or two additions at **108** this opens up a variety of synthetic pathways by combination of allene **100** with various dienophiles.



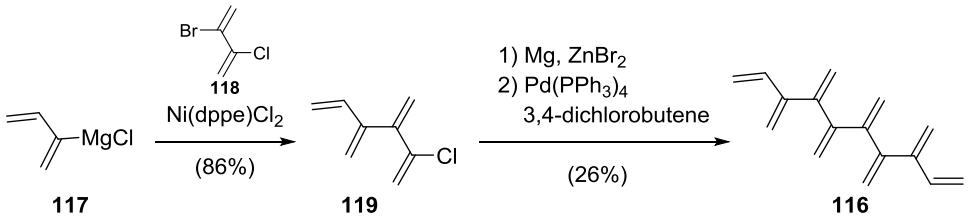
Scheme 17. Reaction of divinylallene **100** with maleimide **106** in a sequence of Diels-Alder reactions.[57]

A class of compounds closely related to divinylallene **100**, are the dendralenes. Actually, the starting material **103** for the synthesis of **100** is a [3]dendralene. Dendralenes are defined as acyclic cross-conjugated polyolefins, which makes 1,3-butadiene the smallest possible member of the class, [2]dendralene.[58] Due to a lack of available methodology at the time, parent dendralenes were long an underdeveloped field.[1] Only in 2000 the group of Sherburn devised a synthetic route to this class of compounds up to [8]dendralene (**116**).[59] In this building block based strategy the well-established thermolytic unmasking of dienes protected as sulfolenes was employed. In the exemplary synthesis of [8]dendralene (**116**) (Scheme 18), stannylsulfolene **110** was iodinated to **111**. This material was then coupled in a Stille reaction with distannane **112** giving rise to **113** and **114**. The masked dienes were then liberated at 450 °C to yield [6]dendralene (**115**) and [8]dendralene (**116**). UV/Vis analysis of the synthesized dendralenes confirmed the previously assumed nonplanar and nonconjugated structure.



Scheme 18. Synthesis of dendralenes by thermolysis of sulfolenes.[59]

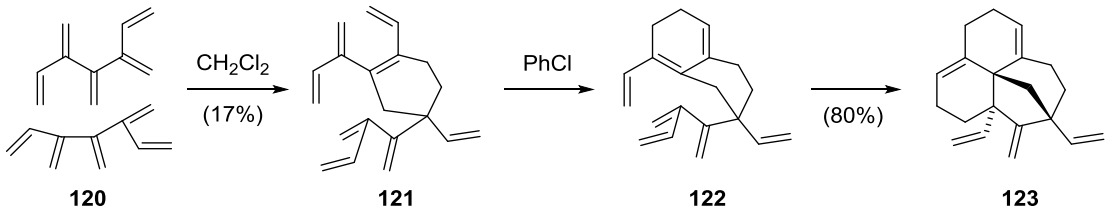
Almost 10 years later an improved synthesis of dendralenes was reported by the same group, allowing to access dendralenes in gram quantities for the first time.[60] In this synthesis simple vinyl- or butadienyl buildings blocks were cross-coupled using Kumada and Negishi conditions. Therefore, no high temperatures and especially no pyrolysis were required as no deprotection step of a sulfolene was involved. Again the synthesis of [8]dendralene (**116**) is shown as an example (Scheme 19). In a Kumada coupling of Grignard **117** with dihalogenide **118** functionalized [4]dendralene **119** was obtained. This was dimerized to [8]dendralene (**116**) by Grignard formation, transmetalation to zinc and palladium-catalyzed homocoupling. With useful quantities in hand, it was possible to survey the properties of dendralenes and it was found that the even and odd numbered series of dendralenes show significantly different behavior. Whereas the even numbered dendralenes show an increase of the molar extinction coefficient with growing length and are quite unreactive the odd numbered dendralenes show exactly the reverse. This is attributed to the oligo-*s*-*trans*-butadiene structure of the even numbered series, whereas the odd numbered series contains at least on quasi-*s*-cis unit.



Scheme 19. Practical synthesis of [8]dendralene (**116**).[60]

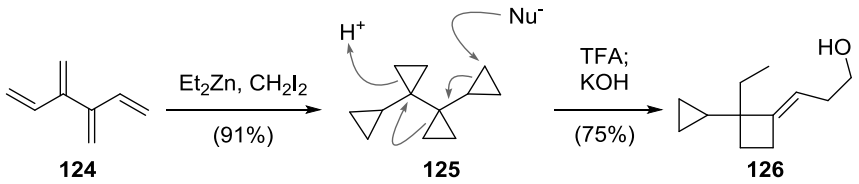
Subsequently the chemistry of dendralenes was investigated. Like divinylallene **100**, the dendralenes are substrates allowing for diene-transmissive Diels-Alder reactions. Therefore it was found that chiral dendralenes could be used to rapidly access enantiopure polycycles in this manner [61] or that for some dendralenes the regioselectivity (internal vs. terminal) of the dienophile attack could be controlled by careful tuning of the amount of the used Lewis acid catalyst.[62] As one example for the power of

dendralenes in domino reactions the dimerization of [5]dendralene (**120**) is shown (Scheme 20).[63] In an intermolecular diene-transmissive Diels-Alder reaction [5]dendralene dimerizes to **121**. Upon heating of this species an electrocyclization to **122** occurs which directly undergoes an intramolecular Diels-Alder reaction to afford fenestrane **123**.



Scheme 20. Synthesis of fenestrane **123** from dendralene **120** in two steps.[63]

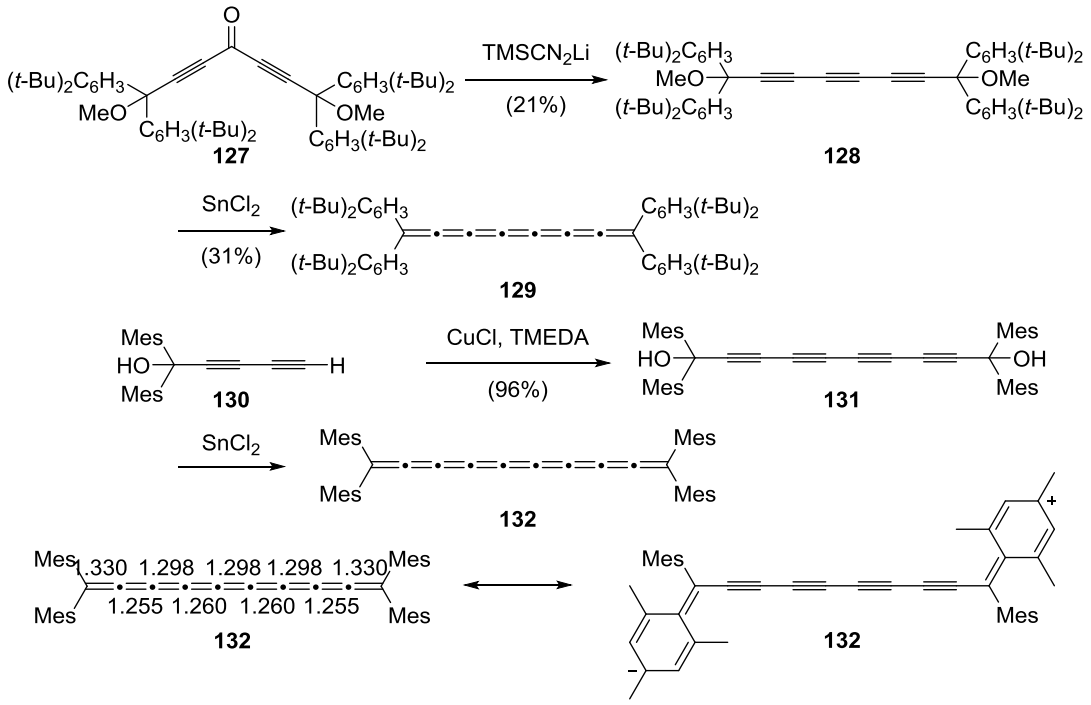
Furthermore, the applicability of dendralenes in organic chemistry was shown in the formal total synthesis of the natural product triptolide.[64] As an aside, Bojase *et al*. synthesized a new family of saturated hydrocarbons by percyclopropanation of dendralenes and named the resulting oligocyclopropanes ivyanes.[65] As a consequence of the synthetically available dendralenes, all family members from [3]ivyane to [8]ivyane were prepared. For example [4]dendralene (**124**) was converted to [4]ivyane (**125**) employing Simmons-Smith conditions (Scheme 21). Single crystal X-ray diffraction experiments showed that the ivyanes adopt helical conformations. In hydrolytic experiments [4]ivyane (**125**) showed cooperative reactivity of the cyclopropane moieties, which could again prove valuable for rapid access to complex molecular scaffolds.



Scheme 21. Synthesis and reactivity of [4]ivyane (**125**).[65]

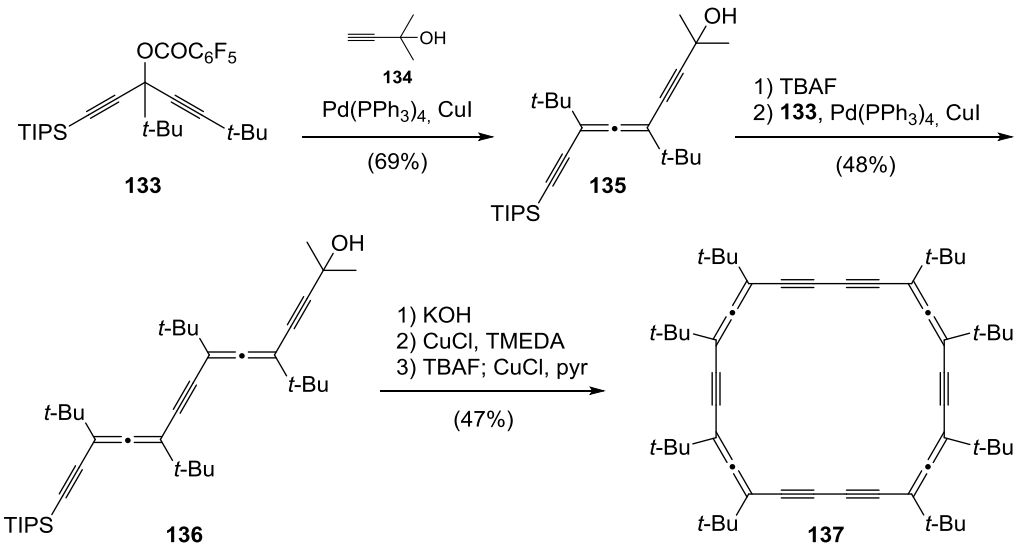
Yet another compound class in hydrocarbon chemistry that has not been explored very thoroughly is the class of cumulenes which describes molecules with more than three directly linked double bonds.[1] The scarcity of experimental information can be attributed to the instability of the higher cumulene homologs, which can only be countered to some extent by introducing stabilizing terminal groups. In 2013 the group of Tykwinsky reported the synthesis of several tetraarylstabilized cumulenes up to [9]cumulenes.[66] The synthesis of [7]cumulene **129** began with the conversion of ketone **127** to triyne **128** in a Fritsch-Buttenberg-Wiechell reaction (Scheme 22).[67] Subsequent reduction with $SnCl_2$ afforded the desired [7]cumulene **129**. In the synthesis of [9]cumulene **132**, homocoupling of alkyne **130** was performed using Hay conditions affording **131**.[68] The cumulene **132** was again obtained by a reduction of alkyne **131**. Single crystal X-ray diffraction data from [3]cumulenes to [9]cumulenes showed the cumulenic structures to be completely linear as opposed to oligoacetylenic structures.

Additionally this analysis pointed out a decrease of the bond length alternation with increasing length of the chain as was expected from computational studies.[69] This alternation is a consequence of an acetylenic resonance structure of cumulenes as shown for the example of [9]cumulene **132**.



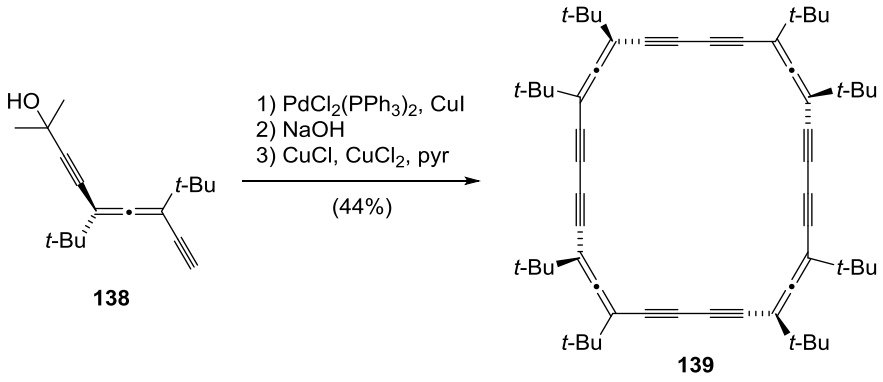
Scheme 22. Synthesis of [7]cumulene **129** and [9]cumulene **132** with a resonance structure of **132** explaining the bond length alternation (with bond length values from single crystal X-ray diffraction).[66]

So far the last building block of hydrocarbon chemistry, the triple bond, was only mentioned in precursor molecules. The next target compound presented also contains triple bonds. In combination of the allene building block with acetylene moieties Odermatt *et al*. created a shape persistent macrocyclic allene **137** (Scheme 23).[70] To this end the methodology for the synthesis of diethynylallenes developed by the group of Diederich was used.[71] Thus, in a palladium-catalyzed cross-coupling of precursor **133** with alkyne **134** diethynylallene **135** was obtained. Silyl deprotection and another cross-coupling with **133** afforded bisallene **136**. After removal of the acetone derived protecting group, homodimerization and subsequent ring closure employing Hay conditions[68] afforded macrocycle **137** in a mixture of two pairs of enantiomers and 3 achiral diastereomers. The mixture was separated into distinct compounds by HPLC using Buckycatcher columns. However, separation of the enantiomers was not achieved. Macrocycle **137** is of interest as a host molecule and due to expectedly unusual chiroptical properties.



Scheme 23. Synthesis of a shape persistent allene macrocycle.[70]

After the development of an enantioselective synthesis of diethynylallenes,[72] the way was paved for a route to enantiomerically pure allene macrocycles. Accordingly, the group of Diederich synthesized macrocycle **139** as a single enantiomer, starting from enantiomerically pure diethynylallene **138**, in a three step sequence of palladium-catalyzed homocoupling, deprotection and Eglinton coupling (Scheme 24).[73] The computationally predicted D_4-symmetric crown structure of macrocycle **139** was substantiated by NMR spectroscopy. More importantly, allene macrocycle **139** showed a huge Cotton effect which was attributed to synergistic geometric and electronic properties.

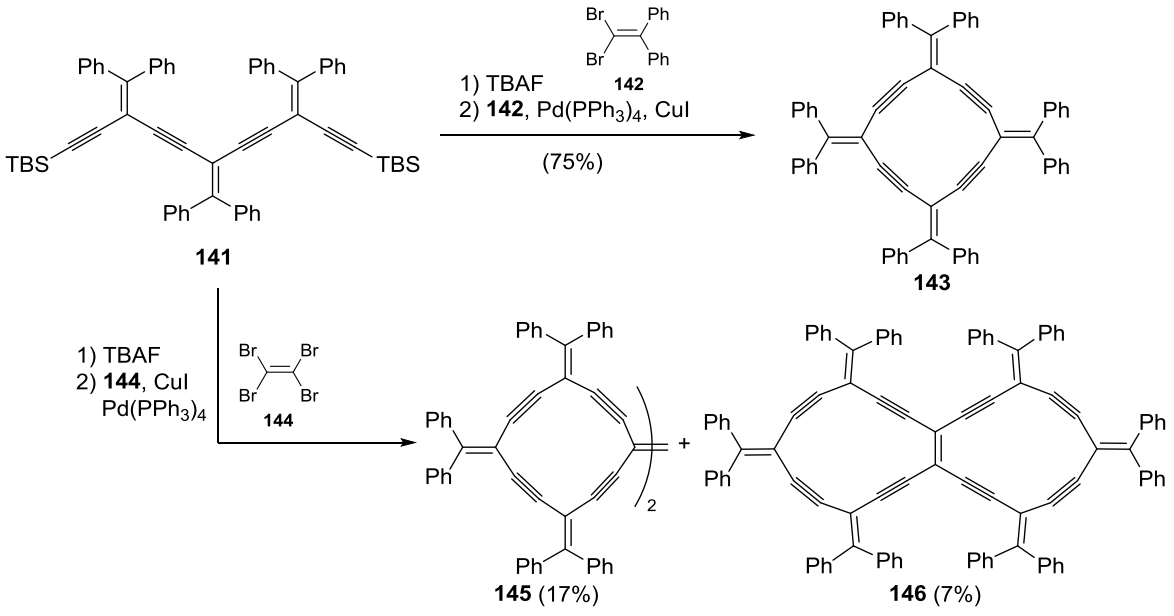


Scheme 24. Synthesis of enantiomerically pure macrocycle **139**.[73]

In macrocycle **139** the triple bonds, presumably, are linear as the molecule can adopt a stable crown conformation. In the extended radialenes the conformation is locked in a planar arrangement due to different bond angle requirements and strain is evident in the distorted geometry of the contained triple bonds. The family of radialenes can be viewed as cyclized dendralenes since formal cleaving of one single bond of a [*n*]radialene compound leads to a [*n*]dendralene, as shown for [5]radialene (**140**) (Scheme 25). The compound class is well established and a variety of radialenes are known, although [5]radialene (**140**) has not been synthesized to date.[1]

Scheme 25. Relationship of radialenes and dendralenes shown in the example of [5]radialene (**140**).

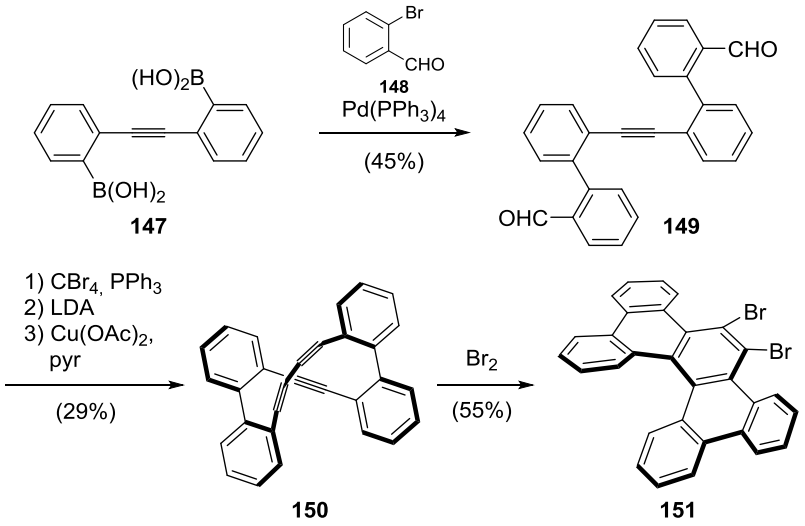
As pioneered by Diederich and coworkers,[74] the radialene scaffold can be expanded by formal insertion of acetylene units into the single bonds, thereby conserving the radialene geometry and giving rise to the extended radialenes. The group of Tykwinsky was the first to report the synthesis of [*n*]radialenes extended by *n*-acetylene units.[75] Building on their work on perphenylated enyne oligomers like **141**,[76] which also can be viewed as an extended [3]dendralene, Gholami *et al*. succeeded in synthesizing extended radialenes in two steps (Scheme 26).[77] Extended radialene **143** was obtained after deprotection of **141** in a twofold Sonogashira reaction with **142** in good yield, whereas Sonogashira reaction with tetrabromoethylene (**144**) gave rise to bisradialene **145** and radiaannulene **146**. By employing the Sonogashira reaction the extended [3]radialene to [6]radialene systems were obtained, demonstrating the ability of this cross-coupling method to access very strained systems. The strain is evident in the distortion of the alkyne bond angle to values as low as 166.7° which makes for a substantial deviation from the ideal 180°, as established by single crystal X-ray diffraction studies.



Scheme 26. Synthesis of extended radialenes, bisradialenes and radiaannulenes.[77]

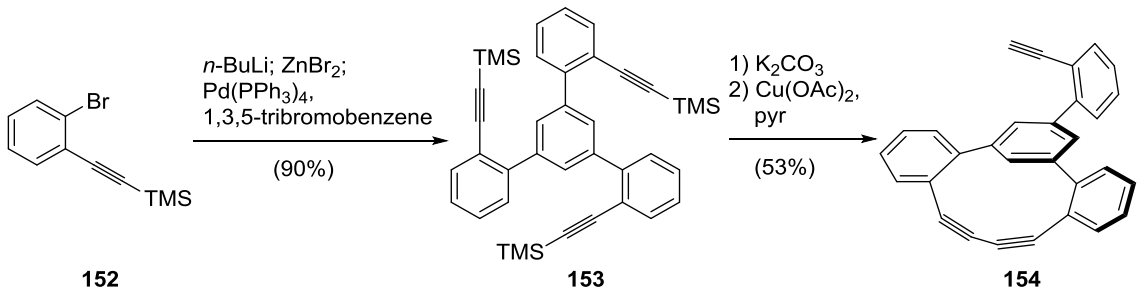
In building with the alkyne functionality the distorsion of the linear bond geometry is of special interest resulting in intensive research on cycloalkynes.[1] Only two examples of distorted alkyne moieties beside the already shown radialenes shall be given. The group of Tobe reported the synthesis of strained diacetylene **150**, with a bond angle as low as 159.3° at the diacetylene moiety (Scheme 27).[78] The synthesis commenced with double Suzuki coupling of diboronic acid **147** with

bromobenzene **148**. Subsequently, dialdehyde **149** was transformed via Corey-Fuchs alkynylation and copper-mediated coupling to distorted diacetylene **150**. Due to the high strain in the compound, it was possible to react it by a bromination reaction at room temperature to afford [5]helicene **151**.



Scheme 27. Synthesis of a highly distorted diacetylene **150** and its conversion to [5]helicene **151**.[78]

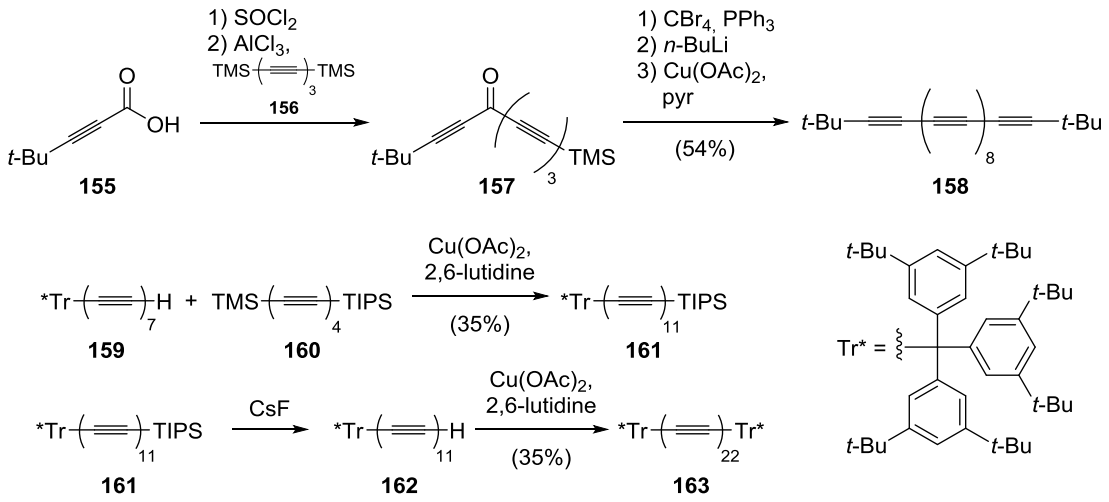
Collins *et al*. reported with **154** an even more distorted molecule containing a diacetylene (Scheme 28).[79] This compound was found serendipitously by the authors as they originally planned to synthesize a cyclophane with diacetylene spacers. Starting from bromobenzene **152**, lithiation, transmetalation and Negishi cross-coupling with 1,3,5-tribromobenzene afforded triyne **153**. Upon subjecting **153** to a variety of coupling conditions, which was planned to result in the dimeric cyclophane, only intramolecularly coupled diacetylene **154** was obtained. This diacetylene displayed a minimum angle of 153.5° and as a result a well-known strain-related downfield shift of the carbon atoms of the acetylene bridge in the ^{13}C NMR spectrum.



Scheme 28. Serendipitous synthesis of diacetylene bridged **154** displaying a highly distorted alkyne moiety.[79]

Another fascinating hydrocarbon class results when only the alkyne moiety is used as a building block. Due to the limited, linear binding situation only rod-like oligomers can be built, ultimately leading to a yet experimentally unrealized carbon allotrope, carbyne. These polyacetylenes are typically very reactive, which leads to the already mentioned use of bulky stabilizing groups. With this strategy, several oligoacetylenes were synthesized and characterized.[1] In a systematic approach, the group of

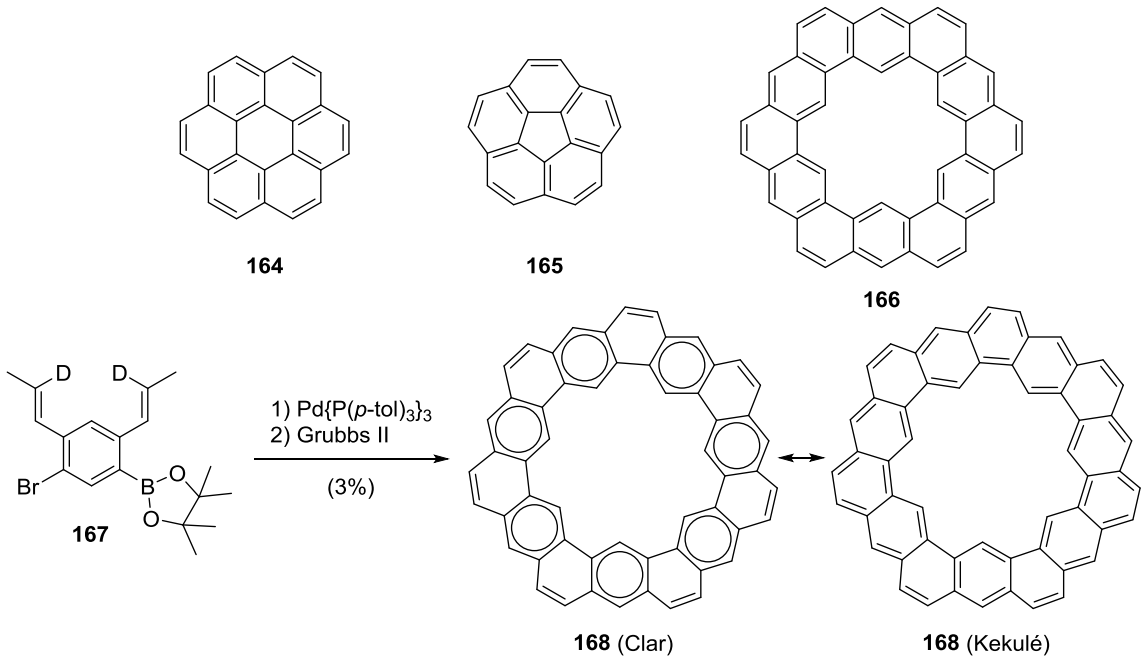
Tykwinski was able to synthesize a range of *tert*-butyl stabilized oligoynes (Scheme 29).[80] The synthesis was designed using several alkyne building blocks with the *tert*-butyl moiety as a stabilizing group, reducing the effect of this group on the sp-carbon chain. In a typical example, propiolic acid **155** was activated and coupled with triyne **156** to result in tetrayne **157**. This was converted in a Corey-Fuchs reaction with subsequent homocoupling to decayne **158**. Using this method, oligoynes with 2, 3, 4, 6, 8 and 10 alkyne units were obtained, that were analyzed by single crystal X-ray diffraction. Analysis showed a slight S-shape for the oligoynes and indicated a decrease of the bond length alternation, as already seen in the isomeric cumulene system (Scheme 22). In a related study by the same group using an explicit modular strategy oligoynes containing from 4 up to 22 alkyne units, such as in **163**, were achieved in sequential Hay or Eglinton-Galbraith couplings of silylated building blocks.[81] In this approach, a very bulky modified trityl group allowed for the stabilization of the long alkyne chains. From the series of the synthesized oligoynes the bandgap of potential carbyne was extrapolated to be 2.56 eV and from the reasonable stability of even very long oligoynes it was deduced that carbyne might be synthetically viable.



Scheme 29. Synthesis of oligoynes using building block based approaches.[80]

1.4 Arenes

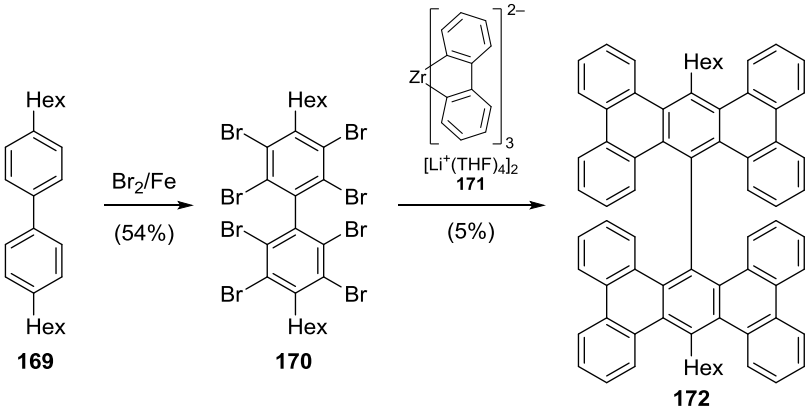
The last category of hydrocarbon compounds to be discussed is not directly evident from one of the three building blocks mentioned in section 1.1. Rather, aromatic compounds are built up from sets of six olefinic building blocks, thereby leading to planar aryl rings with cyclic delocalized electrons, which are also the major characteristics of this compound class. To investigate these characteristics, especially in larger systems than isolated aryl rings, has been the topic of interest in this area of hydrocarbon chemistry for a long time. This resulted in the very early syntheses of extended benzenoid structures like coronene (**164**) in 1932[82], corannulene (**165**) in 1966[83] and kekulene (**166**) in 1978[84] (Scheme 30). Recently the group of King reported the synthesis of the heptagonal analog of kekulene (**166**) and termed it septulene (**168**).[85] The starting material **167** was designed containing a methyl substituent and deuterium label on the vinyl group. This suppressed spontaneous polymerization and allowed for spectroscopic reaction monitoring of the ring closing step. From the Suzuki coupling of monomer **167**, beside polymeric material, also a cyclic heptamer was isolated which was cyclized in a ring closing metathesis to septulene (**168**). Examination of spectroscopic data as well as single crystal X-ray diffraction studies proved unambiguously that the π-electrons of **168** are localized in individual rings as proposed by Clar and not in a concentric array of annulenes as proposed by Kekulé.



Scheme 30. Benzenoid structures coronene (**164**) and kekulene (**166**) and synthesis of septulene (**168**).[85]

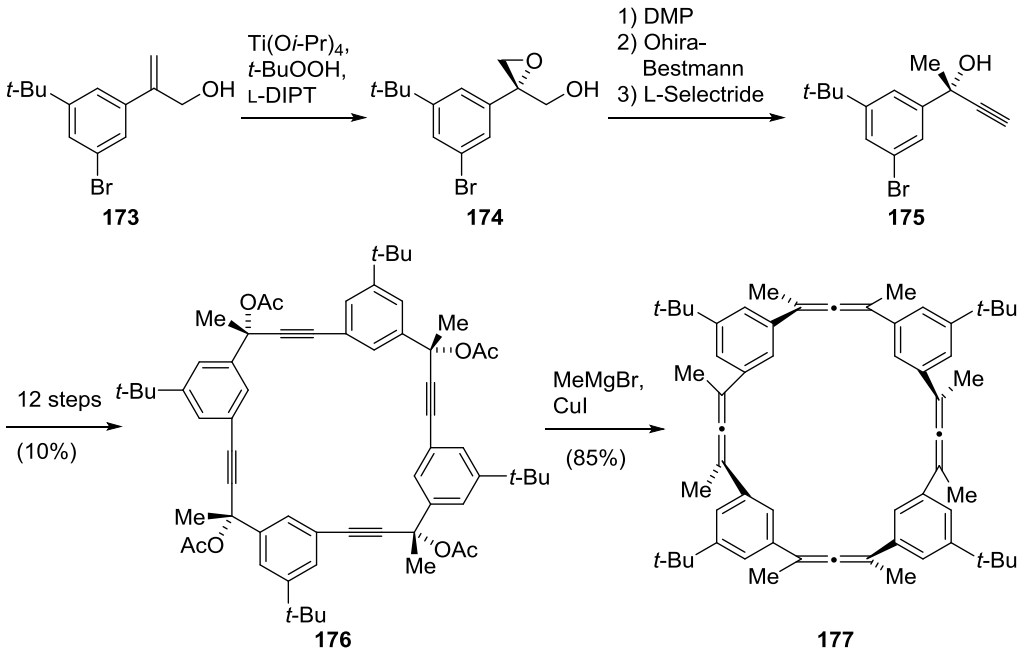
As mentioned earlier, planarity, as a factor of aromaticity, is of special interest in the present compound class. Later in this section several examples will be shown where considerate violation of the planarity of aromatic compounds occurs. One particular example was reported by Hilton *et al*. in dimeric compound **172** (Scheme 31).[86] This compound was obtained from the fourfold coupling of octabromide **170** with zirconium reagent **171**, albeit in low yield. Octabromide **170** itself was perpared

by exhaustive bromination of bisphenylene **169**. Biaryl **172** displays the first so-called gulf-gulf bond reported to date (a highly sterically hindered single bond). Despite the apparent steric strain, this bond is only slightly elongated to 1.49 Å which was reasoned by the authors to be a result of the slow release of strain with bond length extension. Instead, strain is released by a twisting of the aromatic systems resulting in an average torsion angle of 69° as exemplified by single crystal X-ray diffraction.



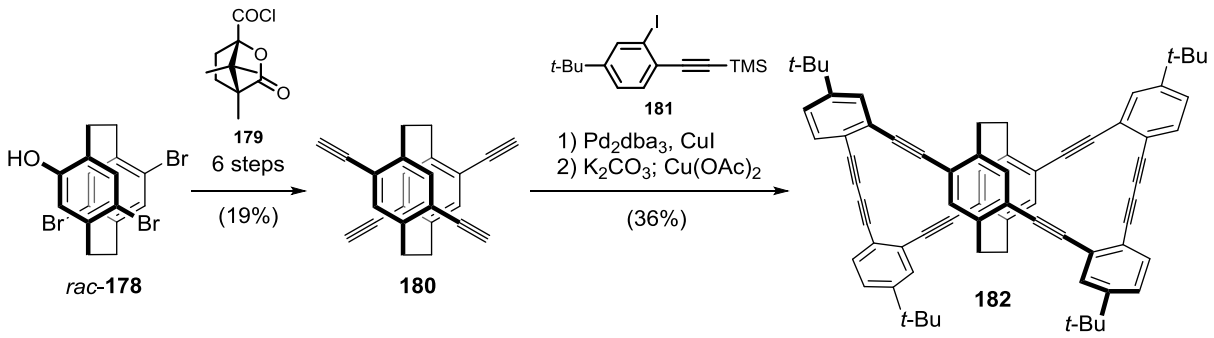
Scheme 31. Synthesis of biaryl **172**, a highly twisted aromatic compound.[86]

In cyclophanes the distortion of the aromatic ring arises by a bridge that tethers two non-adjacent ring carbons. Of late, several groups grew interested in synthesizing chiral cyclophanes. For an access to chiral allenophanes, the group of Fallis developed a method using the Sharpless epoxidation to achieve enantioselectivity (Scheme 32).[87] Thus, allylic alcohol **173** was converted to epoxide **174** enantioselectively. With a sequence of oxidation, homologation and selective epoxide opening enantiopure propargylic alcohol **175** was obtained. Dimerization, functional group interconversions and ring closure resulted in cyclophane **176**. Finally, chiral allenophane **177** was generated in a selective S_N2' methyl cuprate addition.



Scheme 32. Enantioselective synthesis of allenophane **177** employing a Sharpless epoxidation.[87]

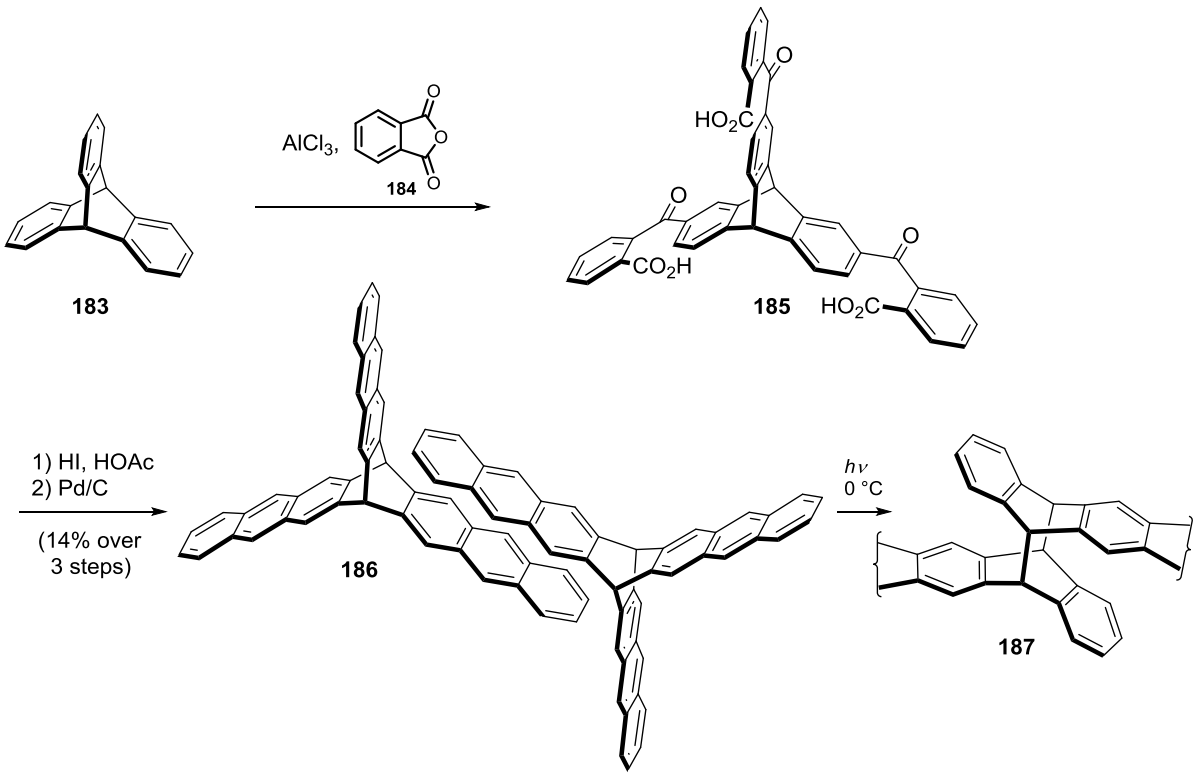
In contrast to the late stage generation of the cyclophane moiety in the previous synthesis, Morisaki *et al*. started out with a cyclophane and developed a method for the optical resolution of **178** using camphanoyl chloride **179** (Scheme 33).[88] The enantiomerically pure material was elaborated to tetraalkyne **180** which was then converted in sequential Sonogashira and oxidative couplings to propeller shaped cyclophane **182**. Due to its planar chirality, cyclophane **182** displayed a large dissymmetry factor as evident from circularly polarized luminescence measurements.



Scheme 33. Enantioselective synthesis of cyclophane **182** using an optical resolution.[88]

A special reason for interest in [*n*,*n*]cyclophanes is the interaction of the aromatic moieties which arises from their close proximity due to their fixed spacial arrangement. Another compound class which attracted interest owing to the setup of the aromatic groups is the class of triptycenes. In these compounds aryl groups point outward from a central bicyclo[2.2.2]octane motive. The group of King recently reported the synthesis of a two-dimensional polymer based on anthraceno triptycene **186** (Scheme 34),[89] which was synthesized in an optimized procedure analogous to the report by Long

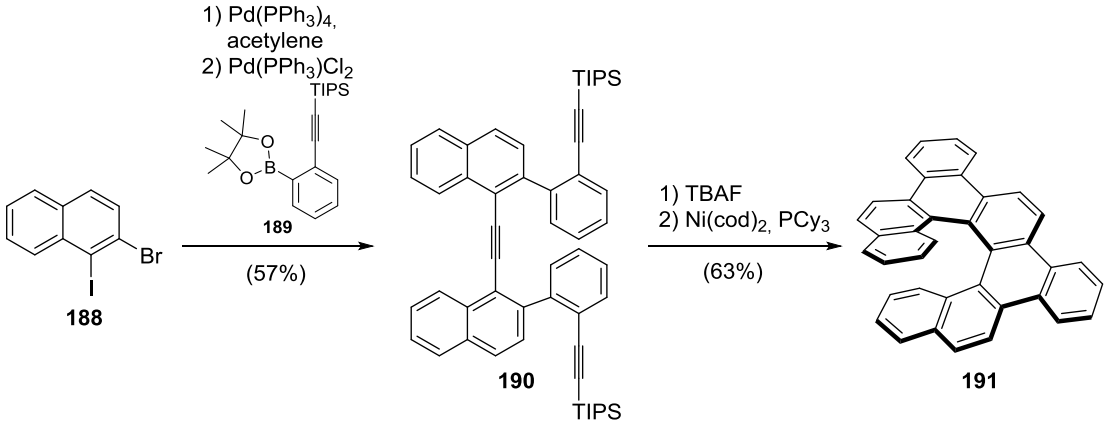
and Swager.[90] Therefore, triptycene **183** was reacted in a Friedel-Crafts acylation with **184** to result in triacid **185**, which was then cyclized and dehydrogenated to give triptycene **186**. Crystallization from benzene afforded a polymorph of **186** which displayed π-π stacking of the anthracene moieties with an average spacing of 4.0 Å. Irradiation of this material **186** with light in the solid state led to cross-linking of the aligned anthracene groups resulting in the two-dimensional polymer **187**. Spectroscopic analysis established a honeycomb structure for this polymer. Depolymerization was observed at elevated temperatures and proved the identity of the building blocks.



Scheme 34. Synthesis of triptycene based two dimensional polymer **187**.[89]

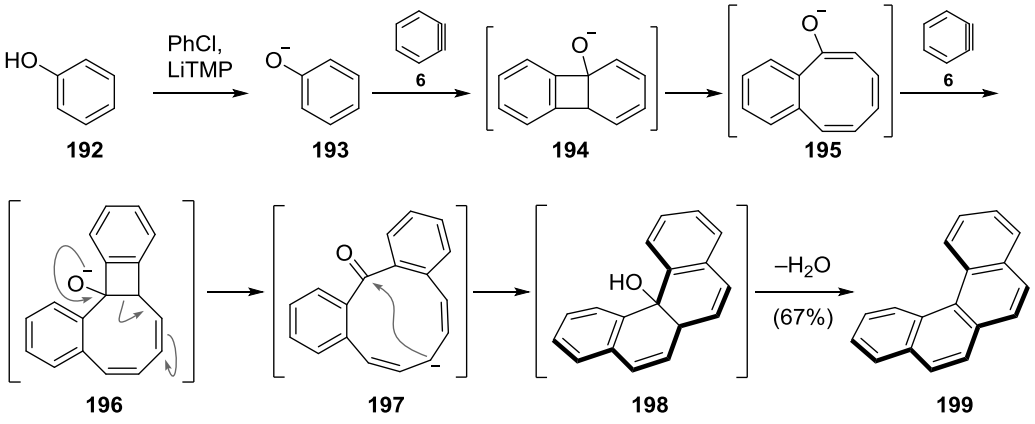
In anthraceno triptycene **186** the aromatic system results from linear annulation and therefore presents a blade-like structure. In the case of angular annulation two possibilities exist for systems containing more than 5 aromatic rings. One way is that the macrocycle gets closed like already seen in coronene (**164**) and corannulene (**165**) resulting in approximately planar systems (Scheme 30). In the second option the aromatic system gets distorted so that one terminus avoids the other. The resulting compound class is called helicenes and attracted interest due to their inherent helical chirality. In 2013 the group of Starý reported a novel synthetic access to enantiomerically pure dibenzohelicenes relying on a nickel-catalyzed alkyne cycloisomerization.[91] In one example of the modular approach, naphthalene **188** was coupled to a bisnaphthalene with an acetylene spacer, which was subsequently Suzuki coupled with **189** to precursor **190** (Scheme 35). After deprotection, this material was converted in the keystep to [7]helicene **191**. The variation of the building blocks allowed for the practical synthesis of a variety of fully aromatic [5]-, [6]- and [7]helicenes. Employing a chiral ligand

in the alkyne cycloisomerization step an enantioselective synthesis with an enantiomeric excess up to 99% was achieved after purification by recrystallization.



Scheme 35. Novel approach to dibenzohelicenes employing a cycloisomerization reaction.[91]

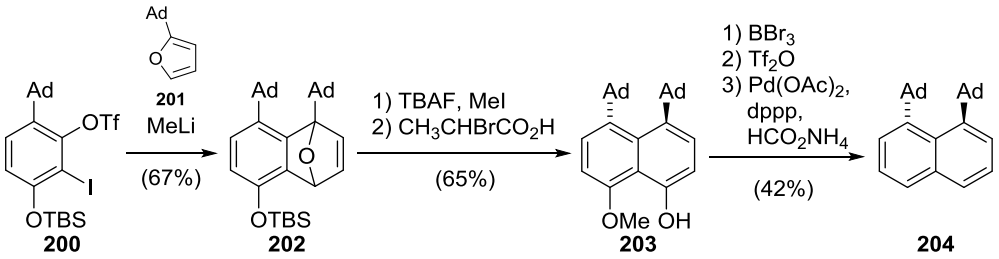
Recently, a remarkable one-step synthesis of [4]helicenes from commercially available starting materials was reported by Truong and Daugulis (Scheme 36).[92] In this approach phenol (**192**), was reacted with in situ generated benzyne (**6**). From the study of reaction intermediates the authors were able to formulate a reaction mechanism. In the proposed mechanism a cycloaddition of benzyne (**6**) with phenolate (**193**) occurs to result in cyclobutene **194**. A 6π electrocyclic ring opening reaction led to **195** which reacted with a second equivalent of benzyne (**6**) to give intermediate **196**. In a vinylogous keto-enol tautomerization this fragmented to **197** which cyclized to **198** and dehydrated to afford [4]helicene (**199**) in decent yield. Beside a variety of [4]helicenes, this method also allowed for the synthesis of a [6]helicene.



Scheme 36. One step synthesis of [4]helicene (**199**) from phenol (**192**) and benzyne (**6**).[92]

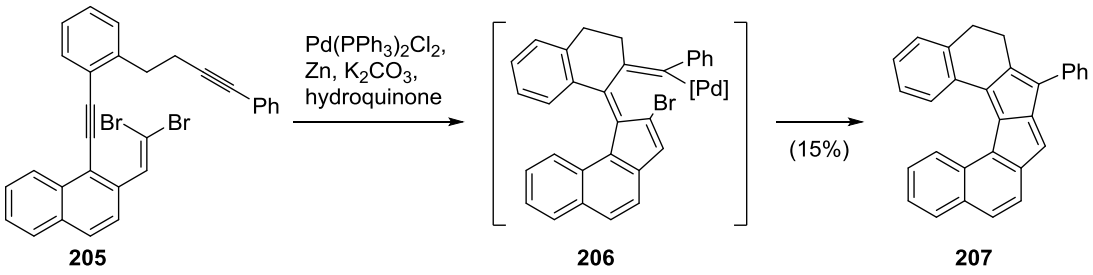
The synthesis of higher helicenes up to [14]helicene has been accomplished.[1] In their synthesis of equatorenes, Aikawa *et al*. investigated the other direction: the smallest possible helicene.[93] By utilizing a Diels-Alder reaction of a benzyne generated from **200** with furane **201**, tricycle **202** was accessed (Scheme 37). This was converted in a reprotection and subsequent ring opening reaction to

equatorene derivative **203**, which was defunctionalized in a three step sequence to parent equatorene **204**. Optical resolution with camphanoyl chloride **179** at the stage of phenol **203** allowed for the enantioselective synthesis of **204**. Due to the gross distortion of this naphthalene, as evident in the dihedral angle of 71.6° of the bonds to the two adamantyl residues, this system can be contemplated as a formal [2]helicene. Despite the high torsion, the aromaticity of the system is maintained and the molecule is configurationally stable. In UV/Vis spectroscopy a considerable red-shift of the absorption maximum, as compared to naphthalene, was observed for equatorene **204**.



Scheme 37. Synthesis of equatorene **204**, a formal [2]helicene.[93]

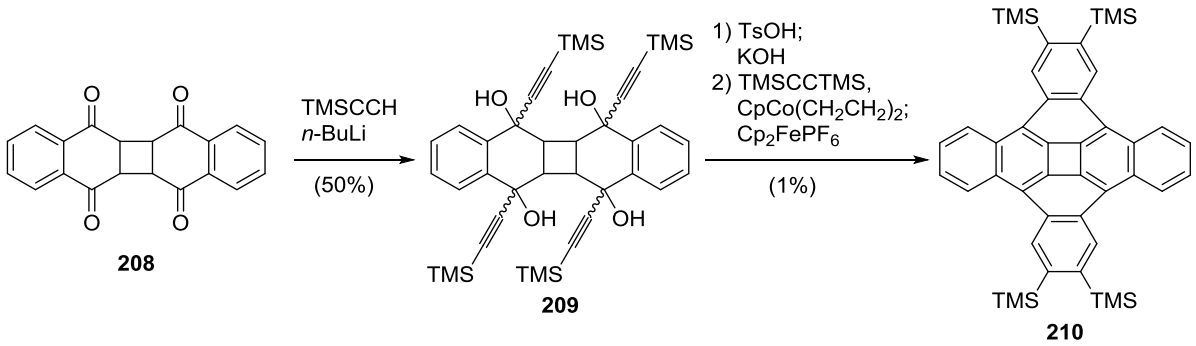
The first anti-aromatic helicene structure was reported recently by the group of Diederich.[94] For the synthesis of these pentalene-based molecules a carbopalladation cascade developed previously in the same group was employed.[95] Thus, geminal dibromide **205** was reacted in a double carbopalladation reaction to intermediate **206**, which under the reaction conditions cyclized to anti-aromatic pentalene **207** (Scheme 38). These novel pentalene helicenes displayed a small HOMO-LUMO gap and redox amphoterism, as a result of their anti-aromatic structure.



Scheme 38. Carbopalladation cascade allowing for the synthesis of pentalene helicene **207**.[94]

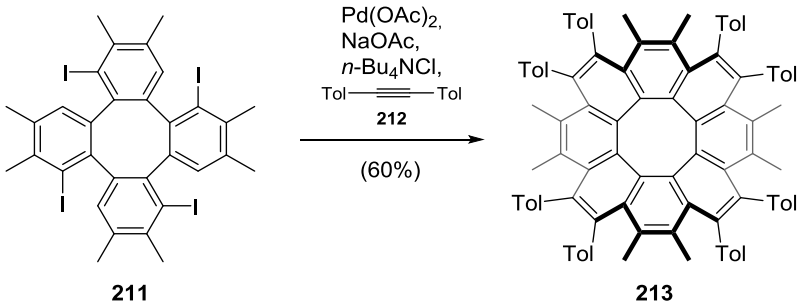
As already mentioned, macrocyclic structures as well as helical structures, can arise from angular annulation of arenes. The resulting compound class is termed circulenes and two examples, coronene (**164**) and corannulene (**165**), which were the first members of the family to be synthesized, were already shown in Scheme 30. Whereas coronene (**164**) is a planar compound, corannulene (**165**) displays a bowl shape with a bowl-depth of 0.87 Å. Continued interest in corannulene (**165**), due to its curved geometry and its relationship to fullerene (**31**), led Siegel and coworkers to establish a kilogram-scale synthesis for this compound.[96] Also only recently [4]circulene and [8]circulene compounds were realized experimentally. In their synthesis of [4]circulene derivative **210**, Bharat *et al*. started out with the addition of lithiated TMS-acetylene to quinone **208** (Scheme 39).[97] The

resulting adduct **209** was converted after deprotection and elimination in a double cyclotrimerization with bis(TMS)-acetylene to quadrannulene **210**. Single crystal X-ray diffraction of [4]circulene **210** established a bowl shape exhibiting a bowl-depth of 1.36 Å. To set this in context: this value is 1.5 times as large as the bowl-depth reported for corannulene (**165**).



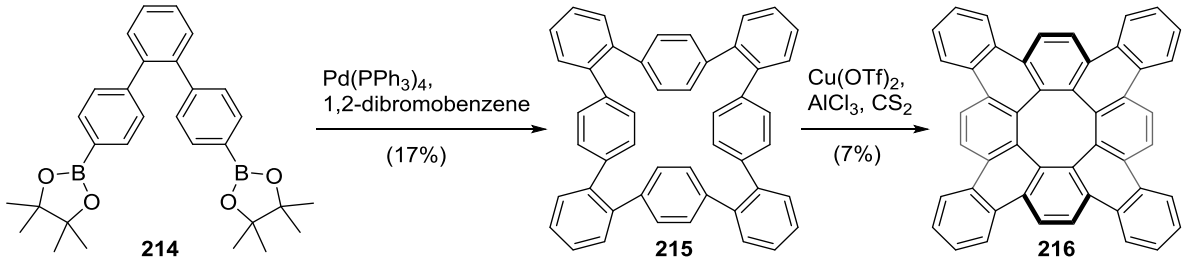
Scheme 39. Synthesis of [4]circulene **210** using an alkyne cyclotrimerization keystep.[97]

Although the first attempt to synthesize [8]circulene was already reported in 1976,[98] it was not until 2013 that remarkably two groups independently succeeded in synthesizing an [8]circulene system. The group of Wu prepared 16-fold substituted [8]circulene **213** in a one-pot carbopalladation over alkyne **212** and subsequent C-H activation cyclization from tetraiodo compound **211** (Scheme 40).[99] In this sequence a yield of 60% was achieved which is quite remarkable, if one considers that the reaction cascade has to occur at four sites of **211** to generate the desired [8]circulene **213**. Single crystal X-ray diffraction displayed a saddle-shape for this compound containing the [8]radialene structure.



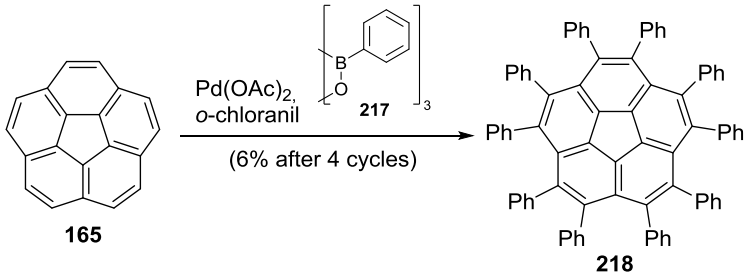
Scheme 40. First synthesis of an [8]circulene compound.[99]

Shortly thereafter the group of Suzuki reported the synthesis of tetrabenzo[8]circulene **216**.[100] This circulene was obtained in a fourfold Suzuki coupling of diboronate **214** with 1,2-dibromobenzene to afford cyclophane **215**, followed by cyclization in a low-yielding Scholl reaction (Scheme 41). Circulene **216**, like **213**, was shown to exist in the saddle-shape by single crystal X-ray diffraction. The group of Whalley established a second synthetic route to circulene **216** and confirmed Clar's concept of individual aromatic systems in such compounds.[101] This fact was reasoned to be responsible for the stability of this circulene, as the presumably reactive olefinic sites are incorporated in the aromatic systems of the additional 4 fused benzene rings.



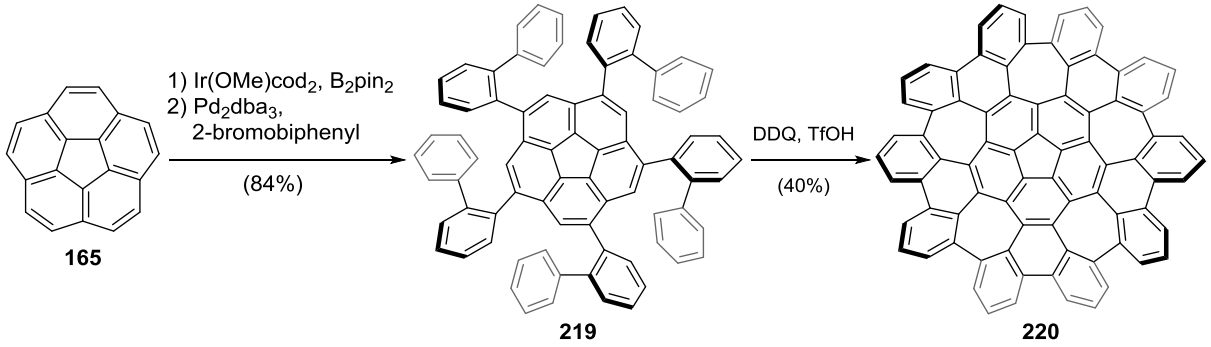
Scheme 41. Synthesis of tetrabenzo[8]circulene (**216**) employing a Scholl reaction.[100]

Owing to their polycyclic aromatic structure with varying degrees of distortion, the compound class of the circulenes bears a close relationship to fullerenes and graphenes. This is especially obvious in corannulene (**165**) and coronene (**164**) which are structural building blocks of C_{60} (**31**) and graphene respectively. In studies to functionalize corannulene (**165**) using C-H activation conditions, the groups of Itami and Scott observed the formation of highly sterically congested decaphenylcorannulene (**218**) and even higher branched systems (Scheme 42).[102] Compound **218** displayed an extraordinary flattening of the corannulene bowl-shape resulting in a bowl-depth of only 0.25 Å, which is less than a third of the value observed for corannulene (**165**). This nearly planar compound can thus be contemplated as a nanographene with a ring defect in the center.



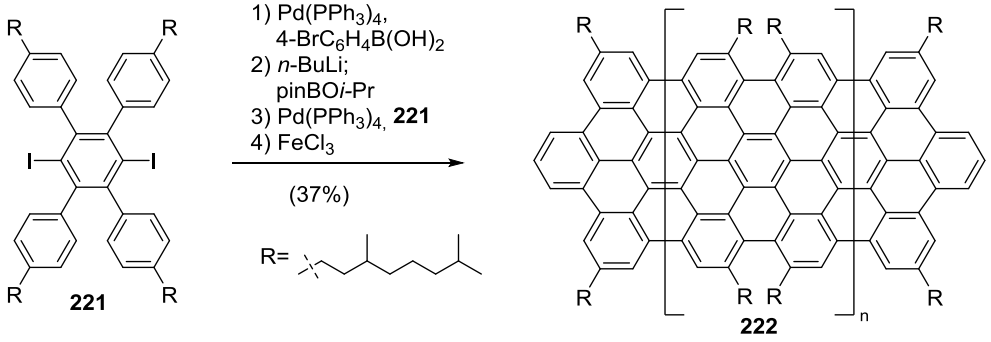
Scheme 42. Synthesis of a flattened corannulene moiety by perphenylation of corannulene (**165**).[102]

Subsequently this concept was extended to larger systems.[103] Therefore, corannulene (**165**) was functionalized as the pentaboronate which was then coupled with 2-bromobiphenyl using Suzuki conditions to afford **219** (Scheme 43). Submitting this material to dehydrogenation conditions resulted in the formation of highly distorted nanographene **220**. The ring defects, present in one five-membered and five seven-membered rings, not only lead to the curved geometry of compound **220** but are also responsible for some unusual properties. These include solubility in common organic solvents, green fluorescence and a relatively large HOMO-LUMO gap. Despite being configurationally stable and chiral in the solid state, **220** racemizes in solution and the mechanism has been resolved computationally.



Scheme 43. Synthesis of warped nanographene **220**.[103]

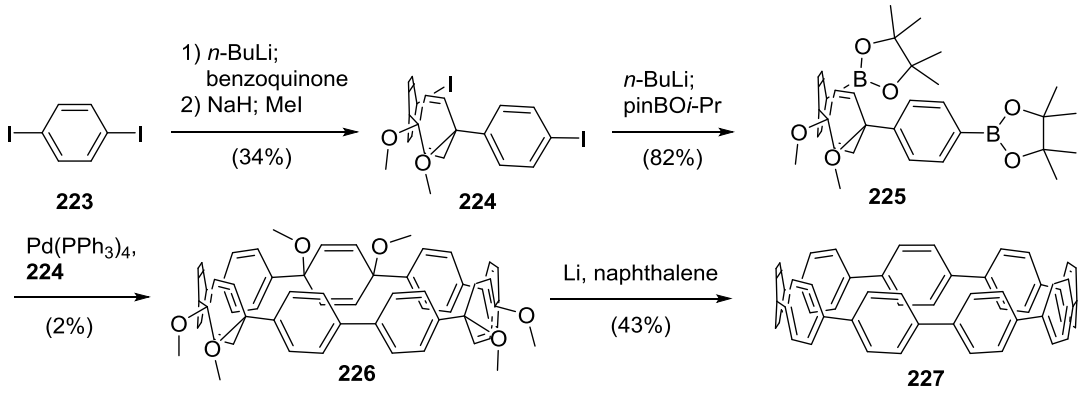
Already before the isolation of graphene in 2004[104] the synthesis of graphite substructures was an intensely investigated area in hydrocarbon chemistry[1] and led to nanographenes with as much as 222 carbon atoms.[105] Efforts to obtain planar nanographenes of defined size and topology were of course bolstered by this report and were pursued with renewed vigour. In 2008 the group of Müllen reported a new method for the synthesis of graphene nanoribbons (Scheme 44).[106] This synthetic protocol, which proceeded from diiodide **221** by a Suzuki cross-coupling, functionalization, polymerization and dehydrogenation using Scholl's conditions, afforded graphene nanoribbons **222** with a low polydispersity. This synthesis allowed for access to defined nanographenes with lengths up to 12 mm which represents the highest advance in a bottom-up approach to nanographenes to date.



Scheme 44. Rational bottom-up synthesis of graphene nanoribbons with low polydispersity.[106]

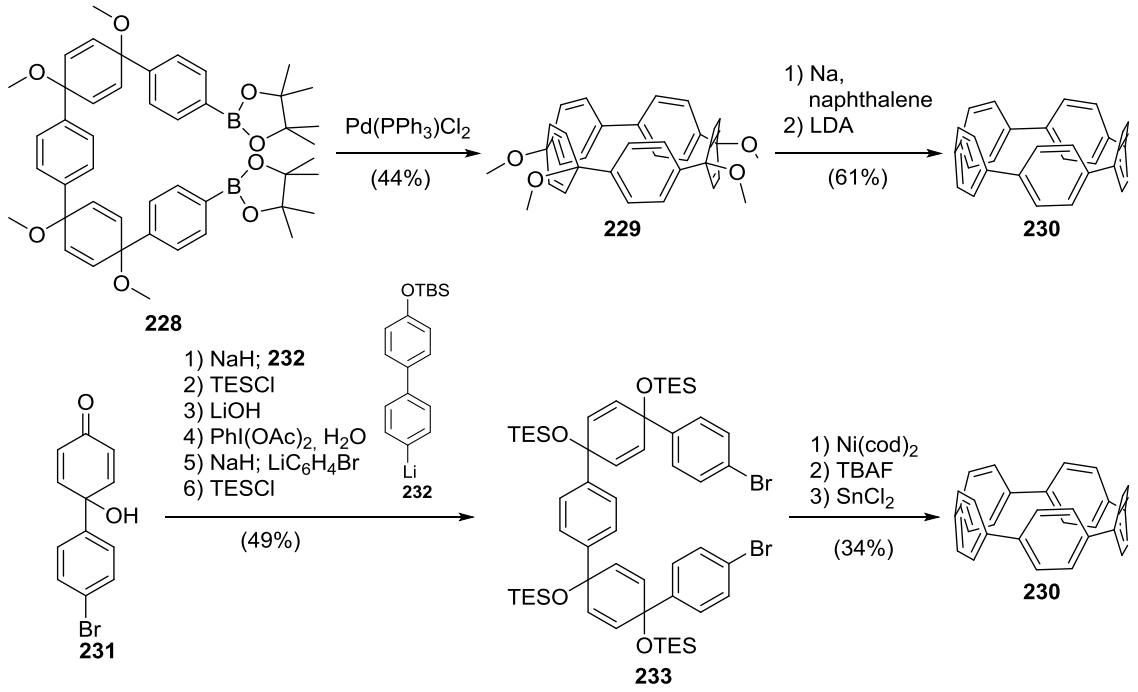
Similarly, considerable work is currently expended toward a rational synthesis of carbon nanotubes especially in respect to a defined diameter. As cycloparaphenylenes constitute the smallest unit of armchair CNTs, research in this area focuses on this compound class. Although first attempts to synthesize cycloparaphenylenes date back to 1934,[107] the group of Bertozzi was the first to develop a method which resulted in the successful synthesis of cycloparaphenylenes.[108] This approach relies on the assembly of bent building blocks into a macrocycle followed by a late stage aromatization step. With this strategy [9]-, [12]- and [18]cycloparaphenylene were synthesized. Exemplary, the synthesis of [9]cycloparaphenylene (**227**) is shown in Scheme 45. In the first step diiodobenzene **223** was monolithiated and reacted with benzoquinone. The resulting diol was dimethylated to diiodide **224** and

then converted to diboronate **225**. In a Suzuki coupling of diboronate **225** with diiodide **224** macrocyclic compound **226** was obtained in low yield. Aromatization under reductive conditions finally gave access to [9]cycloparaphenylene (**227**).



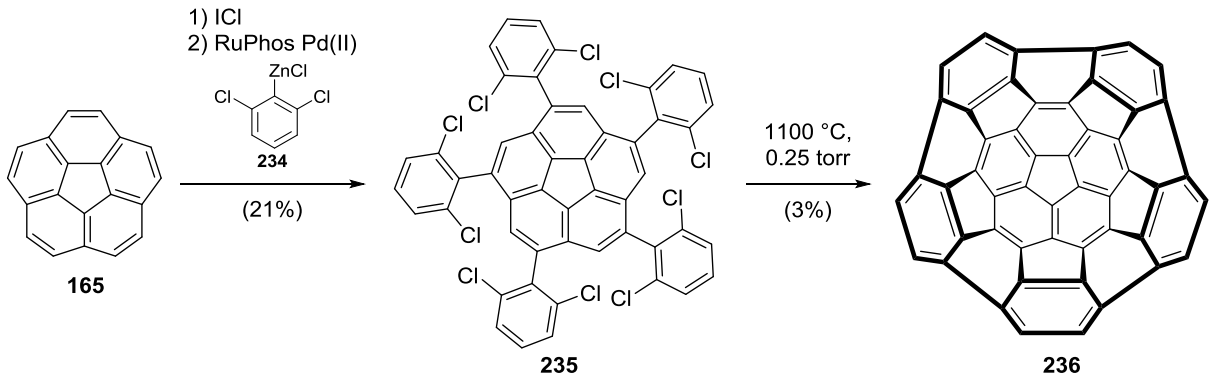
Scheme 45. First synthesis of [9]cycloparaphenylene (**227**).[108]

As a consequence of this successful synthesis, activity in this field increased dramatically and resulted in a flurry of cycloparaphenylene syntheses, giving access from [5]- up to [16]cycloparaphenylene.[109] In the current paragraph only the two most recent independent syntheses of [5]cycloparaphenylene (**230**) shall be presented (Scheme 46). The synthesis by the group of Jasti is reliant on the strategy previously developed by Bertozzi and coworkers.[110] Thus, diboronate **228** was homocoupled resulting in macrocycle **229**. This was then aromatized in two steps by reduction and elimination to the desired [5]cycloparaphenylene (**230**). The approach employed by Yamago and coworkers started with the addition of aryllithium **232** to **231**.[111] After protection, deprotection, oxidation and another lithiumaryl addition a precursor similar to diboronate **228** was obtained. The cyclization step was then achieved using Nickel-catalysis and finally deprotection and reduction afforded [5]cycloparaphenylene (**230**). Interesting from a structural point of view is that the *para*-carbons of the benzene rings in [5]cycloparaphenylene (**230**) are distorted 15.6° out of the plane of the benzene ring, thereby illustrating the immense strain energy in the system. As it turned out, cycloparaphenylene **230** exhibits very small oxidation and reduction potentials which offers promise for an application as an organic semiconductor.



Scheme 46. Independent syntheses of [5]cycloparaphenylene (**230**) by Jasti and Yamago.[110],[111]

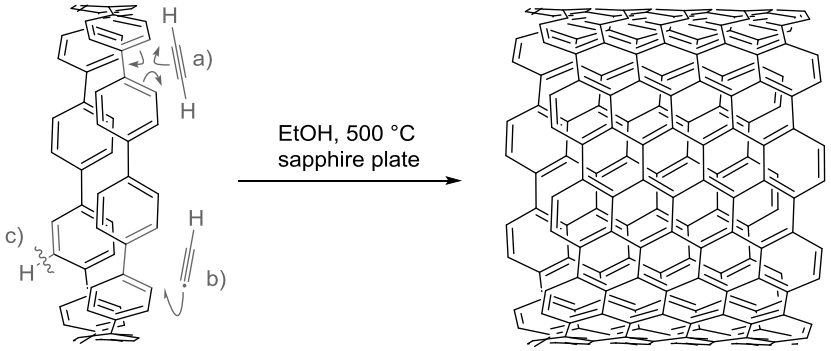
Another important contribution in the investigation of CNT subunits came from the group of Scott which managed to synthesize the end-cap of a [5,5]CNT for the first time.[112] The synthesis started with the pentachlorination of corannulene (**165**) and a subsequent Negishi coupling with zincate **234** resulting in pentaarylated corannulene **235** (Scheme 47).[113] As the FVP reaction was developed substantially by the group of Scott as a tool for the formation of geodesic hydrocarbons,[114] this reaction was also used for the conversion of decachloride **235** into spherical end-cap **236**. Single crystal X-ray diffraction of this species showed a bowl-shape with an immense depth of 5.16 Å and a diameter of ~10 Å for the beginning of the tube.



Scheme 47. Synthesis of the end-cap of a [5,5]CNT from corannulene (**165**).[112]

Building on all these results, Omachi *et al*. searched for conditions that would allow them to grow CNTs from cycloparaphenylenes, therefore giving access to CNTs of defined diameter. Finally, CNTs were successfully synthesized using cycloparaphenylenes on a sapphire plate as the template and

ethanol as an acetylene source at 500 °C.[115] It was shown by the authors that the average diameter of the formed CNTs is dependent on and closely related to the diameter of the used template cycloparaphenylene. As is shown for the exemplary formation of [10,10]armchair CNT **238** from [10]cycloparaphenylene (**237**) in Scheme 48, three mechanisms are currently discussed for this observation. While computational evidence points to a Diels-Alder mechanism (a) or an ethynyl radical addition (b),[116] experimental results indicate that a cycloparaphenylene radical could be generated and react with transiently formed unsaturated C_2 species (c). Investigations in order to elucidate the mechanism are underway, but already these initial results give hope that an access to CNTs of defined size, structure and also chirality might be soon available on a useful scale.



237 **238**

Scheme 48. The first successful bottom-up synthesis of CNTs using cycloparaphenylenes as a template.[115]

1.5 Outlook

Despite continuing interest in the synthesis of classic hydrocarbon structures like tetrahedrane (**9**), [4,4,4,4]fenestrane (**239**) or the infamous tetrakis(*tert*-butyl)ethene (**240**) to name only a few (Figure 8),[1] current interest in hydrocarbon chemistry seems to shift more and more to high molecular weight systems. As shown in the preceding sections, progress has been achieved in the specific synthesis of the basic building blocks of diamond, nanographene or CNTs. Nevertheless, important issues are still unsolved. As yet, the bottom-up approaches to the mentioned polymeric structures have not been applied on a practical scale. Also, only armchair CNTs have been realized in a bottom-up approach. An example for a structural unit of a chiral CNT has been synthesized in acene-inserted cycloparaphenylene **241**.[117] In contrast to this, no cyclacene (like structure **242**) as the smallest building block of a zig-zag CNT has ever been accomplished. Furthermore, a rational approach to graphane (**86**) or nanographanes have yet to be reported in the literature. To resolve these questions will be the task of hydrocarbon chemists in the future.

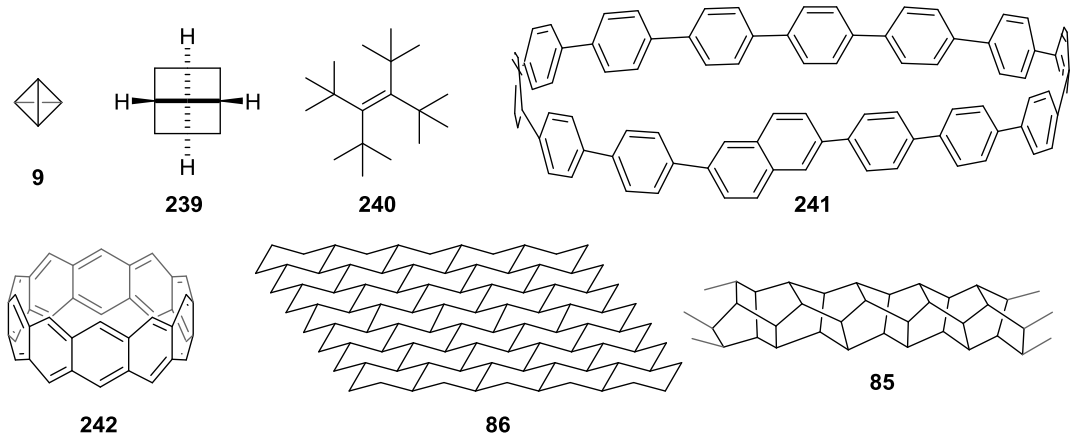


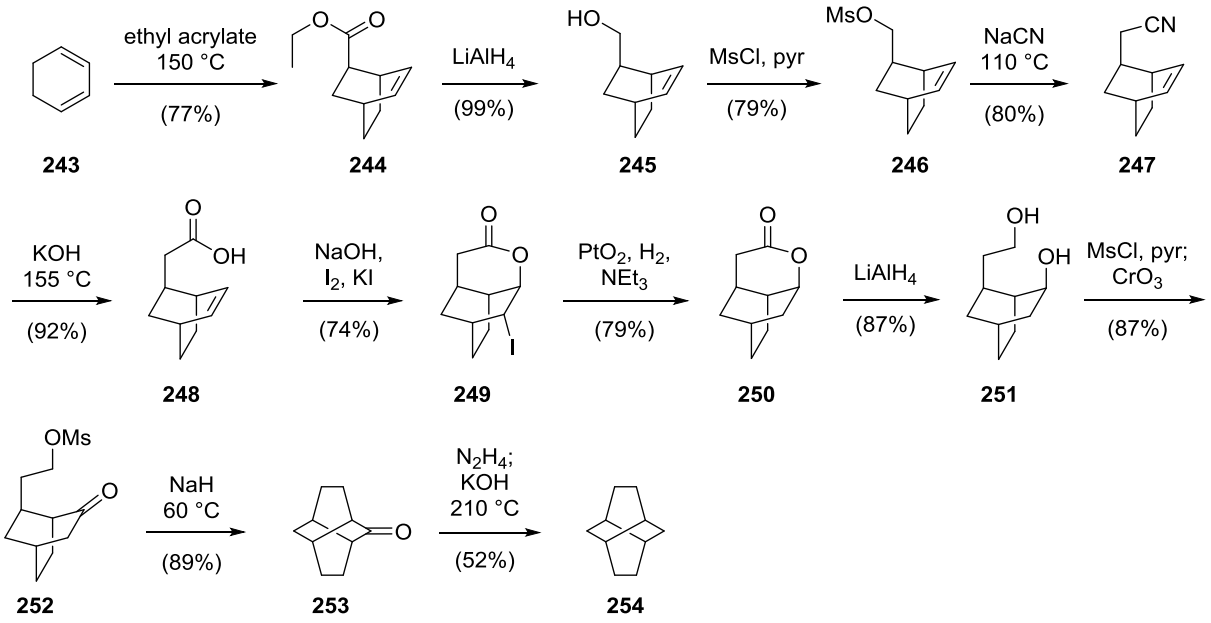
Figure 8. Future targets in hydrocarbon chemistry.

The following thesis presents efforts toward the synthesis of the yet only theoretically existing polymer polytwistane (**85**). For an insight into its spectroscopic properties the synthesis of a short oligomer was conducted (Chapter 2). For the synthesis of polytwistane (**85**), two synthetic routes were investigated but are yet to yield the desired polymer. To allow for the identification of polytwistane (**85**) in complex reaction mixtures the NMR properties of polytwistane (**85**) were determined computationally (Chapter 3). Additionally, work toward the synthesis of twistanamines, which are being synthesized as potential antiviral agents, is reported (Chapter 4).

2 Synthesis of C_2-Tritwistane

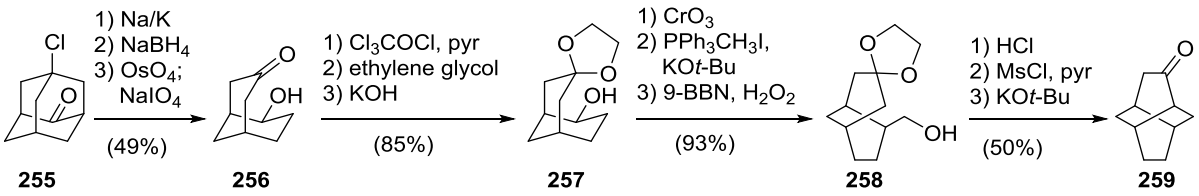
2.1 Background and Aims

Twistane (**254**) is a classic hydrocarbon which attracted interest due to its chirality and inherent strain. Both properties originate from the constituting D_2-symmetric twist-boat cyclohexane moieties. In 1962 Whitlock accomplished the first synthesis of twistane (**254**) using an intramolecular enolate alkylation as the key step to generate the twistane scaffold (Scheme 49).[118] The synthesis commenced with a Diels-Alder reaction of cyclohexadiene **243** with ethyl acrylate resulting in bicyclo[2.2.2]octene ester **244**. After a four step homologation sequence consisting of reduction to alcohol **245**, mesylation to sulfonate **246**, nucleophilic substitution to nitrile **247** and hydrolysis, the homologated acid **248** was obtained. Subsequent conversion to iodolactone **249** followed by hydrogenolytic iodine removal furnished lactone **250**. Reduction to diol **251** then completed the functionalization of the second ethano bridge. In a one-pot monomesylation and oxidation to ketomesylate **252** the stage was set for the generation of the twistane scaffold in the next step. Intramolecular enolate alkylation conditions yielded twistanone **253**, which was defunctionalized to parent twistane (**254**) using the Wolff-Kishner procedure.



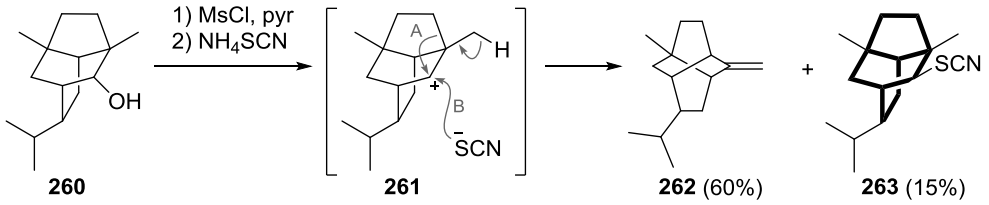
Scheme 49. The first synthesis of twistane (**254**) by Whitlock.[118]

In the following years six other successful approaches were reported for the synthesis of twistane (**254**).[119] The most recent and probably least popular synthesis (Scheme 50) started with a reductive cleavage of chloroadamantanone **255**, followed by reduction and Lemieux-Johnson oxidation to result in ketoalcohol **256**. Protection of the ketone function first required the protection of the alcohol moiety therefore leading to a three step sequence for the conversion to dioxolane **257**. The secondary alcohol was then homologated by oxidation, Wittig olefination and hydroboration to primary alcohol **258**. Deprotection, mesylation and alkylation then yielded the desired twistanone **259**.



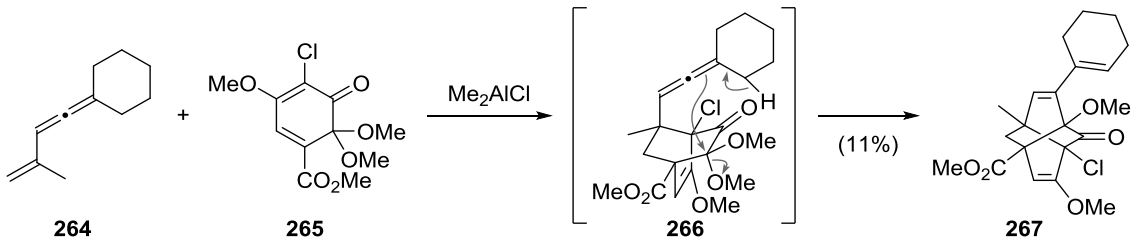
Scheme 50. Formal synthesis of twistane (**254**) by Hamon and Young.[119f]

Later it was found that the twistane skeleton is not only available from total synthesis but also occurs in some natural products.[120] In recent times active efforts to synthesize twistane structures decreased markedly. Nevertheless, twistane structures continue to be reported, often isolated as an unwanted side product and sometimes not even identified as a twistane. These reports yield important insights into possible ways to form the twistane scaffold. For instance it was found in synthetic studies toward natural products containing the pupukeanane skeleton that twistanes were formed under certain conditions. In the last steps of Srikrishna and Gharpure's synthesis of 2-thiocyanatoneopupukeanane (**263**) twistane derivative **262** was formed *via* intermediate **261** along with the desired natural product under S_N1 conditions in a ratio of 4 : 1 in favor of the twistane structure (Scheme 51).[121] This illustrates the high propensity of these tricyclic systems to undergo Wagner-Meerwein rearrangements.



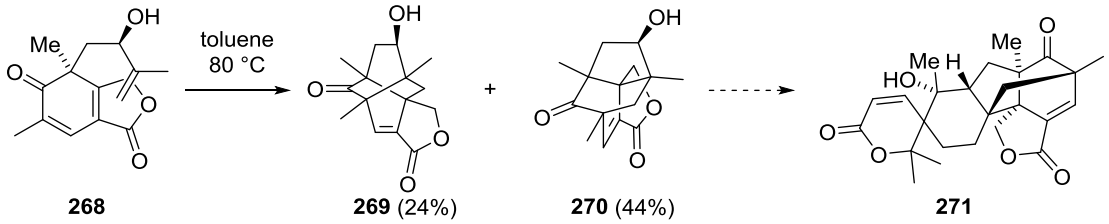
Scheme 51. Formation of twistane derivative **262** (pathway A) in the synthesis of pupukeanane **263** (pathway B).[121] The isotwistane skeleton is highlighted in the natural product.

In synthetic studies toward another pupukeanane natural product, the Lewis acid catalyzed reverse electron-demand Diels-Alder reaction of vinylallene **264** and *ortho*-quinone acetal **265** resulted, *via* intermediately generated allene **266**, in the formation of twistadiene **267** (Scheme 52).[122] This reaction was proposed to occur through an intramolecular carbonyl-ene mechanism, which was facilitated by Lewis acid activation of the dimethylacetal in intermediate **266**. Despite the low yield, this report constitutes a step-economic access to the highly strained twistadiene core.



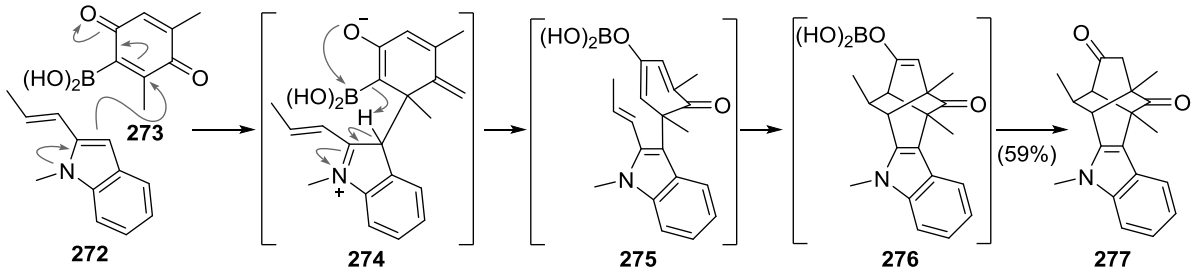
Scheme 52. Formation of twistadiene **267** in a sequence of a reverse electron-demand Diels-Alder and a carbonyl-ene reaction.[122]

Additionally it was found, with the first example being reported by Greuter and Schmid,[123] that the twistane skeleton can be accessed by an intramolecular Diels-Alder reaction if a particular substitution pattern is present in the starting material. This observation stands in contrast to the previous assumption that exclusively the isotwistane scaffold is formed in this reaction.[124] Thus, Spangler and Sorensen observed in their studies toward andibenin B (**271**) that the key intramolecular Diels-Alder reaction of lactone **268** not only afforded the isotwistene skeleton in **270** but also twistene **269** (Scheme 53).[125] However, twistene **269** was converted into isotwistene **270** upon exposure to elevated temperatures displaying that the isotwistene scaffold is thermodynamically favored over the twistene skeleton.



Scheme 53. Formation of twistene **269** as a side product in an approach to the bicyclic core of andibenin B (**271**).[125]

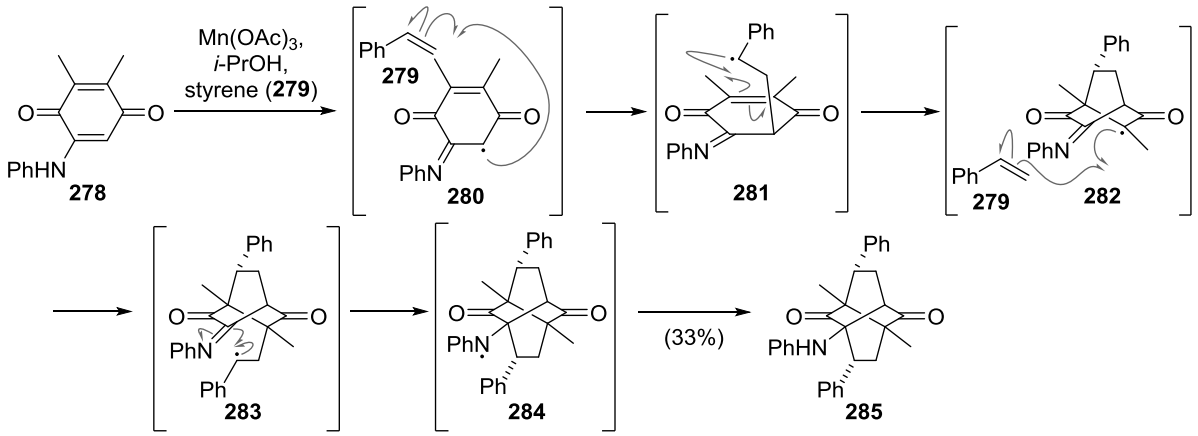
Another example for the mentioned regioselectivity in a Diels-Alder reaction was reported by the group of Carreño in their synthesis of twistenedione **277** by a Michael/intramolecular Diels-Alder cascade (Scheme 54).[126] Supposedly a regioselective Michael attack of indole **272** on *para*-quinone **273** leads to adduct **274**, which upon shift of the boronic acid group is converted to diene **275**. This then undergoes a regioselective intramolecular Diels-Alder reaction to afford twistane **277** after protodeboronation in moderate yield. In this manner, a variety of indoles were reacted to the corresponding twistanes. No formation of the respective isotwistanes was observed. The authors noted that the presence of the boronic acid group in *para*-quinone **273** is essential for the selectivity of the reaction as substrates lacking this moiety led to the isotwistane scaffold.



Scheme 54. Proposed mechanism for the formation of twistenedione **277** in a Michael / intramolecular Diels-Alder cascade.[126]

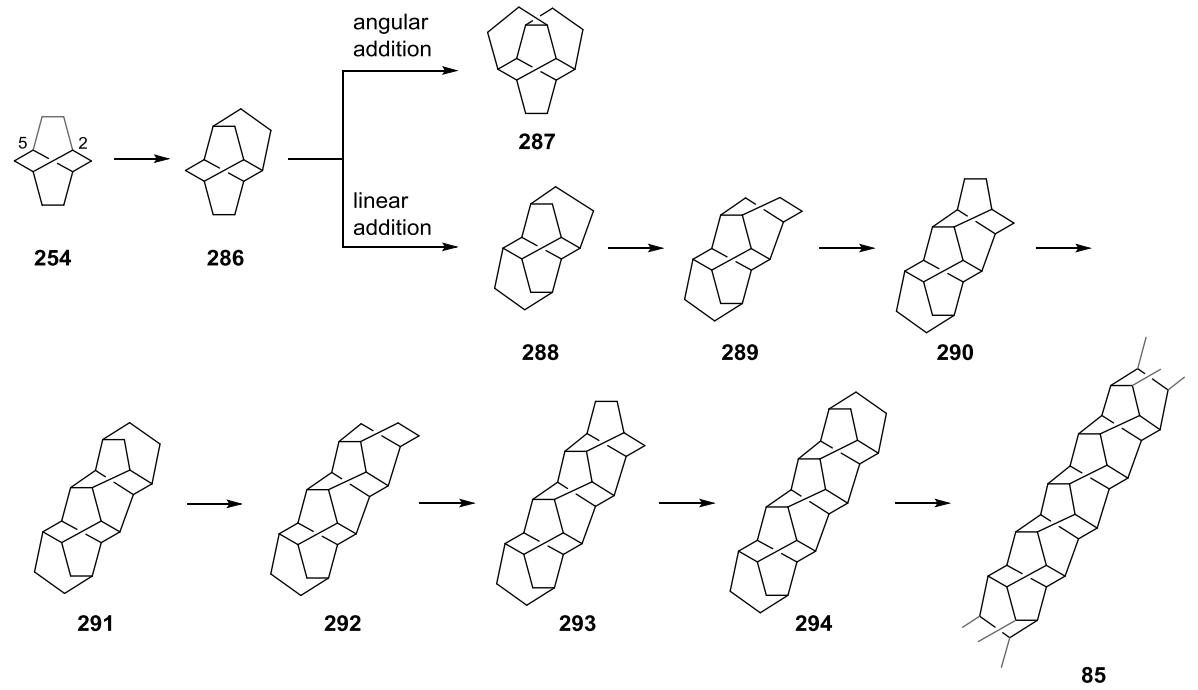
A remarkable formation of the twistane skeleton was reported by the group of Chuang using radical conditions (Scheme 55).[127] In their proposed mechanism, starting from aminobenzoquinone **278**, imine radical **280** was generated using manganese acetate. This radical then reacted in a double 6-*exo*-

trig cyclization with two molecules of styrene **279** *via* bicyclo[2.2.2]octane radical **282** to afford twistanedione **285**, the structure of which was established by single crystal X-ray diffraction. Unexpectedly, no trace of the corresponding 5-*exo-trig* cyclization product was observed. The general 5-*exo-trig* preference of radical cyclizations seems to be circumvented under these conditions.



Scheme 55. Synthesis of twistanedione **285** in a double 6-*exo-trig* radical cyclization.[127]

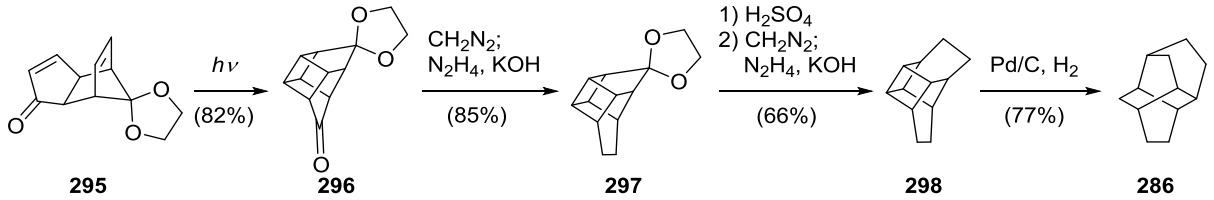
Twistane (**254**) itself can be regarded as a bicyclo[2.2.2]octane with an ethano (ethane-1,2-diyl) bridge between C2 and C5, which locks the twist-boat conformation in the constituting cyclohexane rings (Scheme 56). Extension of twistane (**254**) by another ethano bridge with the respective connectivity results in ditwistane (**286**), conserving the twist-boat conformation in all available cyclohexanes.



Scheme 56. Theoretical generation of oligotwistanes and polytwistane (**85**) from twistane (**254**).

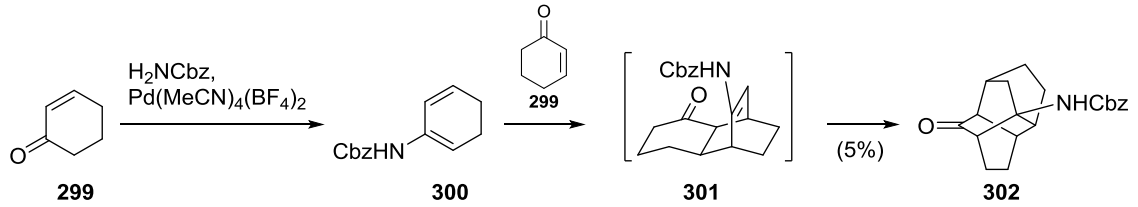
For the next addition of an ethano bridge two possibilities exist: in case of an angular attachment globular D_3-tritwistane (**287**) is obtained whereas a linear extension leads to C_2-tritwistane (**288**). A series of linear ethano additions starting from tritwistane **288** then gives *via* C_2-symmetric tetratwistane (**289**), pentatwistane (**290**), hexatwistane (**291**), heptatwistane (**292**), octatwistane (**293**), nonatwistane (**294**) and so on, ideally in infinity, polytwistane (**85**).

Reports in the literature concerning higher twistanes are scarce, but some routes to the ditwistane scaffold[128] and to parent ditwistane (**286**) have been described.[129] The enantioselective synthesis of ditwistane (**286**) by Nakazaki *et al*. enabled the study of its chiroptical properties and featured a double Tiffeneau-Demjanov type ring expansion (Scheme 57).[130] In the first step of the synthesis, Diels-Alder adduct **295**, which was also available in enantiopure form,[131] was photocyclized to bishomocubane **296**. An ensuing ring expansion with subsequent defunctionalization afforded homobasketane **297**. After deprotection of the acetal moiety, another sequence of ring expansion and deoxygenation yielded dehydrodiwistane **298** which upon hydrogenation gave rise to parent ditwistane (**286**).



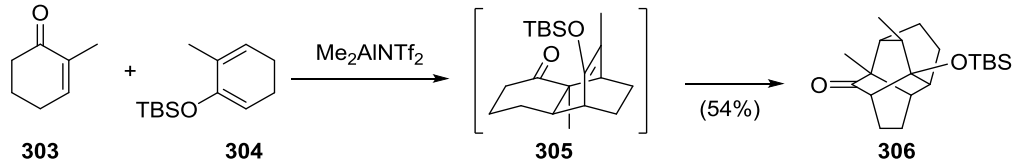
Scheme 57. Synthesis of ditwistane **286** employing Tiffeneau-Demjanov type ring expansion reactions.[130]

More recently, ditwistane **302** was found as a side product by the group of Spencer in their studies of hetero-Michael reactions (Scheme 58).[132] The proposed mechanism for the formation of **302** proceeds *via* 1,2-addition of the amine nucleophile to cyclohexenone **299** resulting in conjugated enamine **300**. This can react further in a Diels-Alder reaction with cyclohexenone **299** to tricycle **301** which upon tautomerization undergoes a Mannich reaction affording ditwistane **302** in low yield.



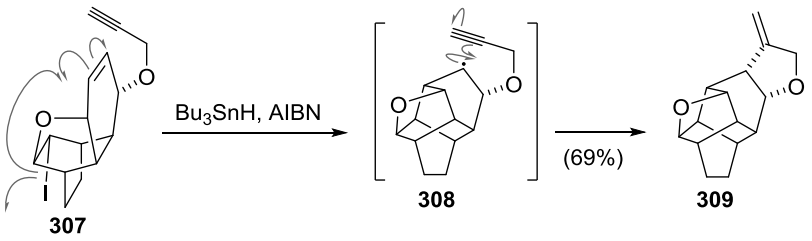
Scheme 58. Proposed mechanism for the formation of ditwistane **302** by a Diels-Alder / Mannich sequence.[132]

In a similar Diels-Alder/aldol cascade Jung and Guzaev observed the formation of ditwistane **306** upon prolonged reaction times (Scheme 59).[133] In this instance, sterically demanding tetrasubstituted diene **303** reacted with trisubstituted dienophile **304** to afford tricycle **305**. Upon activation of the silyl enol ether moiety in **305** an intramolecular aldol reaction then delivered ditwistane **306**.



Scheme 59. Formation of ditwistane **306** in a Diels-Alder/aldol cascade.[133]

A quite efficient access to the ditwistane skeleton was reported by Gharpure and Porwal employing reductive radical cyclization conditions (Scheme 60).[134] Thus, iodoether **307** was cyclized to tetrahydrofurane **309**. The radical originating from iodoether **307** can cyclize on two carbon atoms, but in the reaction exclusively the formation of one product was observed. The classification of the observed cyclization regioselectivity is complicated due to the tetracyclic nature of the starting material. In respect to the tetrahydrofuran ring a 5-*exo-trig* cyclization leads to radical **308**, which is then trapped in a 5-*exo-dig* cyclization resulting in ditwistane **309**.



Scheme 60. Formation of ditwistane **309** under reductive radical conditions.[134]

Regarding oligotwistanes larger than ditwistane (**286**) only the synthesis of branched tritwistane (**287**) was accomplished in the laboratory (Figure 9).[135] This hydrocarbon attracted interest due to the relative orientation of its possible substituents and caused investigation in this area. As a result, the synthesis of a plethora of compounds, of which only triketone **310** and tribenzenannulated derivative **311** are shown, was reported.[136]

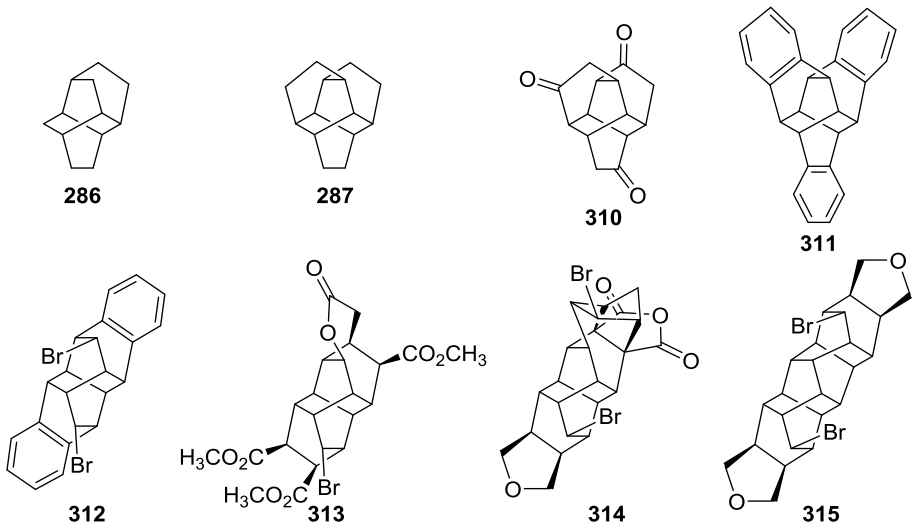
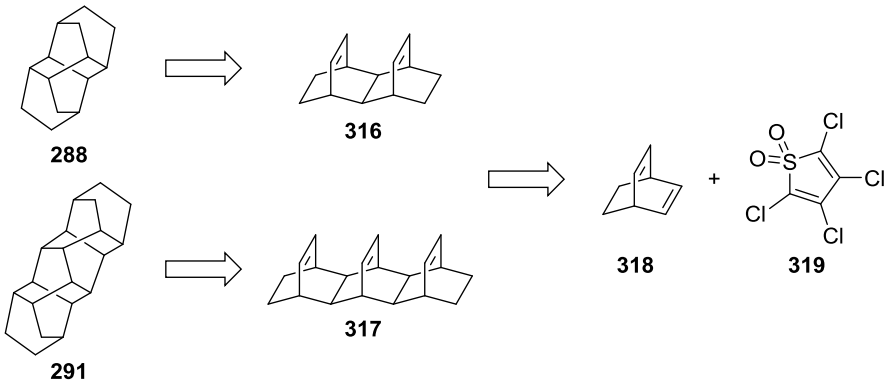


Figure 9. Reported compounds incorporating oligotwistane skeletons larger than ditwistane (**286**).

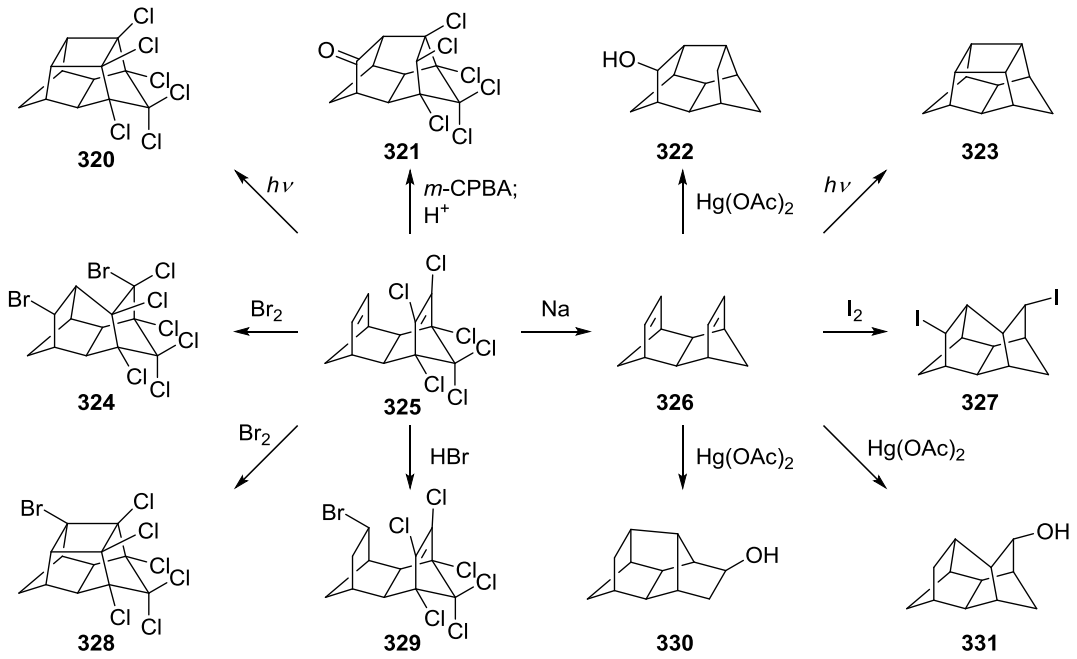
In addition to this, three derivatives of linear tritwistane, dibromide **312**,[137] lactone **313**[138] and dibromide **314**[139] and one molecule incorporating the hexatwistane skeleton, dibromide **315**,[140] have appeared in the literature. All of these higher linear oligotwistanes have a common precursor, the laticyclic conjugated oligoenes, and have been synthesized by electrophilic addition reactions.

In order to extend the series of known linear oligotwistanes and to obtain spectral information which could help later to identify polytwistane (**85**) in complex reaction mixtures (Chapter 3), a synthesis of linear oligotwistanes was pursued in this part of the project. To this end, an electrophilic addition to suitable laticyclic homoconjugated oligoenes was to be exploited, analogous to the syntheses of **312** and **315**. Therefore C_2-tritwistane (**288**) and C_2-hexatwistane (**291**) were planned to be synthesized in electrophilic additions from known laticyclic diene **316** and triene **317**,[141] which were in turn available from dihydrobarrelene (**318**)[142] and thiophene dioxide **319**[143] (Scheme 61).



Scheme 61. Retrosynthetic analysis of twistane oligomers **288** and **291**.

From the work of Lin *et al*. on the related substituted systems **312** and **315** it is known that the crucial electrophilic addition step is highly prone to rearrangements.[137],[140] Such rearrangements in systems of laticyclic conjugated double bonds were investigated thoroughly by the groups of Soloway and Winstein already in 1960.[144] This work was based on isodrine (**325**) which is not only commercially available but can also be seen as a skeletal bisnoranalog of **316**. In these studies several rearranged products were proposed on the grounds of analytical methods available at the time, being essentially IR spectroscopy and mass analysis (Scheme 62). Some of these structures, for example compounds **320** to **323**, were reproduced in later work by other groups,[145] but for other compounds, like **324** and **327** to **331**, no further evidence was ever reported.

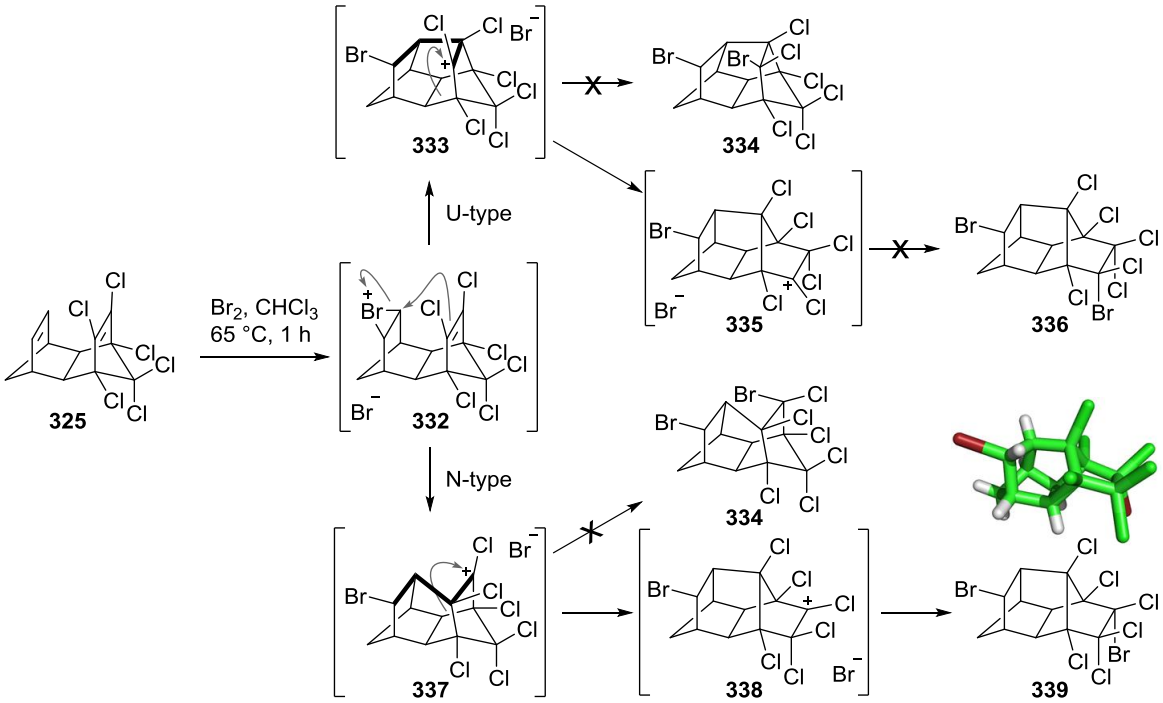


Scheme 62. Products of rearrangements in the system of isodrine (**325**).[144]

Due to its availability and presumably related reactivity isodrine (**325**) was chosen as a model system for the electrophilic addition reaction which was planned to be used as the crucial step for the generation of the oligotwistanes **288** and **291**.

2.2 Studies in Model System Isodrine

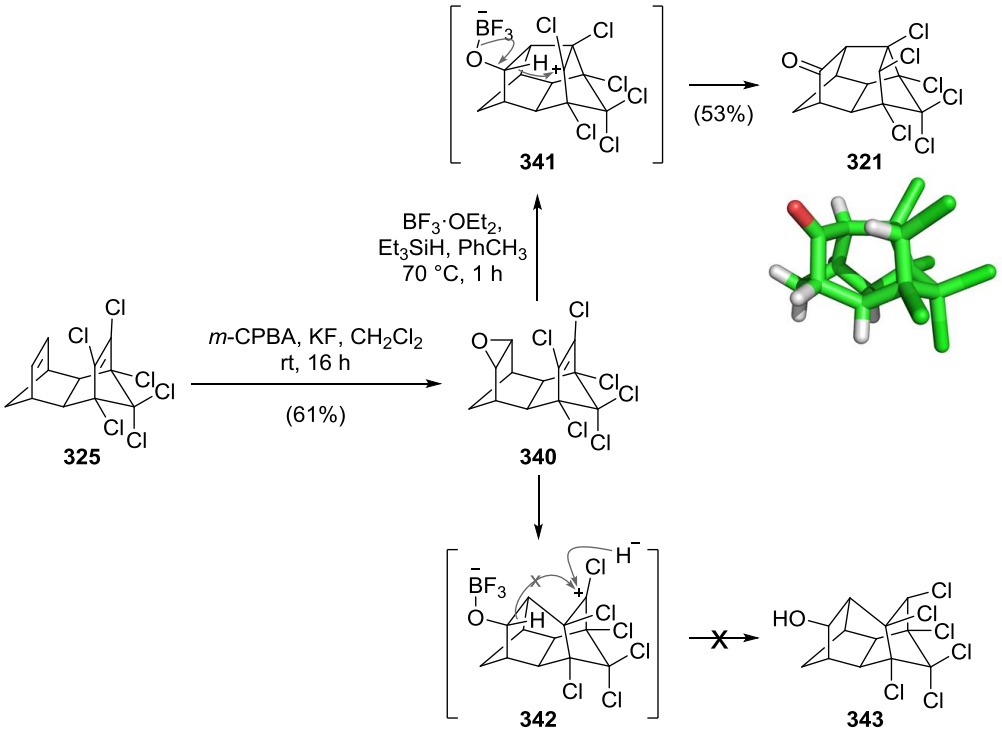
First synthetic work was directed at reproducing the observations by Soloway and Winstein.[144] As the bromination of isodrine (**325**) was reported to give rise to the product of the desired N-type cyclization, dibromide **324**, these conditions were tried out first. Thus, isodrine (**325**) was exposed to bromine to afford one major product beside multiple unidentified compounds, according to ^{1}H NMR, which was purified by recrystallization. Single crystal X-ray diffraction of suitable crystals established the structure of the major product to be dibromide **339** (Scheme 63). For the formation of this product the following mechanism is viable. After the formation of bromonium ion **332** the electronic interaction with the neighboring double bond allows for two pathways. In the case of a U-type cyclization, bromide **333** is generated which can either be directly trapped to result in dibromide **334** or undergo a Wagner-Meerwein rearrangement to bromide **335**, which would then react to dibromide **336**. In the other case, an N-type cyclization, intermediate **337** would be formed. This again could be directly trapped to give the desired dibromide **324** or rearrange to intermediate **338** resulting in dibromide **339**. As dibromide **339** was the only isolable species, the desired cyclization mode seems to be operative. However, carbocation **337** presumably is too sterically hindered to be trapped by a bulky bromide leading to the following rearrangement. As the structure of dibromide **324** was only assigned by Soloway *et al*. based on conformational analysis, it might be reasonable to assume that their isolated compound was in fact also dibromide **339**.



Scheme 63. Proposed mechanism for the bromination of isodrine (**325**) with the X-ray structure of isolated dibromide **339**. The eponymous framework generated by the N-type and U-type cyclization is highlighted.

Next, the conjugate opening of epoxide **340**, which was available from isodrine (**325**) by epoxidation with *m*-CPBA, was investigated.[145] It is known that the Lewis acid catalyzed opening of epoxide **340**

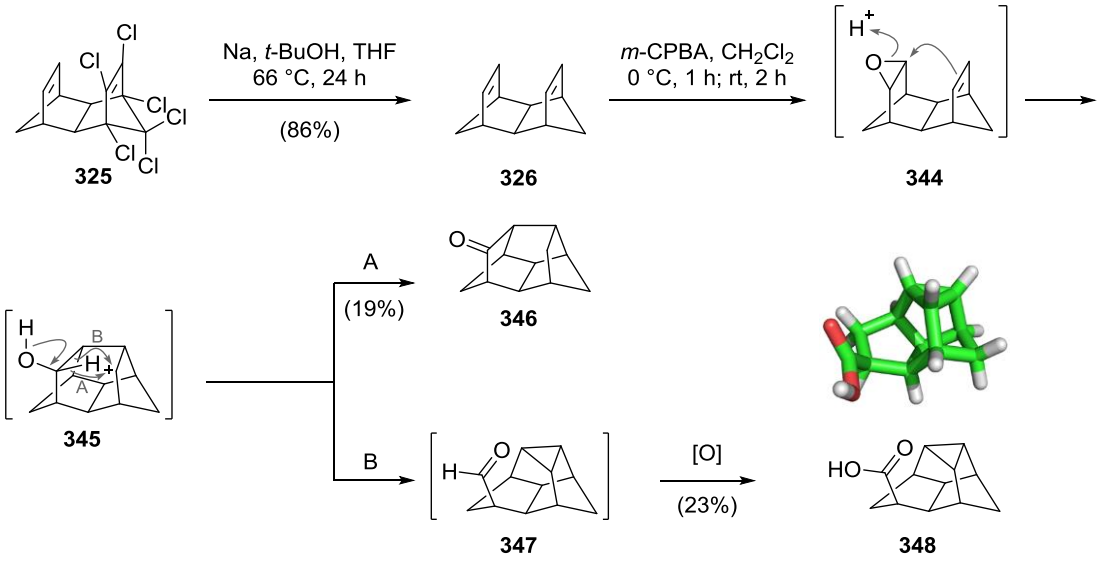
affords ketone **321** after an intramolecular hydride shift of U-type cyclized intermediate **341**.[145] In the case of N-type cyclized intermediate **342** the necessary orbital overlap for such an intramolecular hydride shift is not present and therefore this shift cannot take place. As previously outlined, the product of the bromination reaction implies that the N-type cyclization is viable and maybe even favored over the U-type cyclization. For this reason, it was envisioned that performing the epoxide opening under Lewis acid catalysis with the addition of an external hydride source might enable trapping of intermediate **342** to give access to **343**. Unfortunately, the reaction only yielded known ketone **321** under these conditions (Scheme 64). Employing H_2O as a nucleophile and $InCl_3$ as a weaker Lewis acid in order to establish a thermodynamic equilibrium also only provided undesired ketone **321**. Suitable crystals of this species for single crystal X-ray diffraction were obtained and unambiguously proved the structure of ketone **321**.



Scheme 64. Conjugate opening of epoxide **340** resulting only in ketone **321** as exemplified by its crystal structure.

As steric factors supposedly play a crucial role in the trapping of the cyclization products, dechlorinated isodrine **326** was to be used as a less hindered substrate for the electrophilic reaction. Therefore, isodrine (**325**) was reduced to hydrocarbon **326** using dissolved metal conditions (Scheme 65).[146] Subjecting diene **326** to the same bromination conditions which were used in the case of isodrine (**325**) afforded only a complex mixture of products. Variation of reaction parameters such as temperature, concentration or duration did not give better results. It was not possible to isolate and assign distinct structures from these reaction mixtures.

Next, epoxidation of **326** and subsequent efforts to open the resulting epoxide **344** were to be examined. However, from the ensuing epoxidation reaction only ketone **346** and carboxylic acid **348** were isolated, instead of the expected epoxide **344** (Scheme 65). Presumably, residual chlorobenzoic acid activates the intermediately generated epoxide **344**, resulting in a U-type cyclization to carbocation **345**. This intermediate then can rearrange either *via* a hydride shift to ketone **346** or in a 1,5-alkyl shift to aldehyde **347**, which gets further oxidized to carboxylic acid **348**. The structure of carboxylic acid **348** was proven by single crystal X-ray diffraction. Performing the reaction using a buffered solution or other epoxidation agents did not yield any other product. Interestingly, a literature search for the carbocyclic cage structure of **348** revealed that the hexachloro derivative of **347** has been proposed as a degradation product in gas-liquid chromatography of epoxide **340** and is otherwise unprecedented.[147]

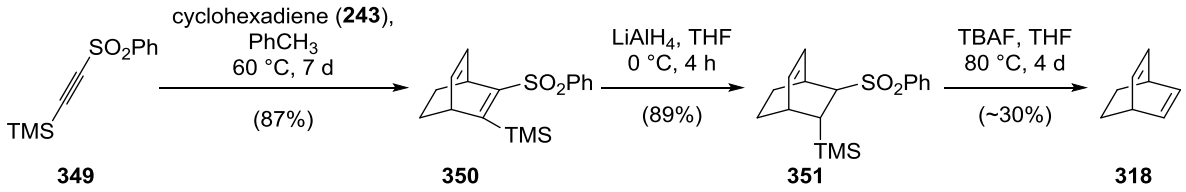


Scheme 65. Efforts toward epoxidation of **326** resulting in ketone **346** and acid **348**, the structure of which was established by its crystal structure.

As the tetracyclic model system was shown to undergo different rearrangements highly depending on geometry and orbital alignment, it was reasoned that further cyclization studies were best conducted on polycyclic systems that can yield the twistane scaffold.

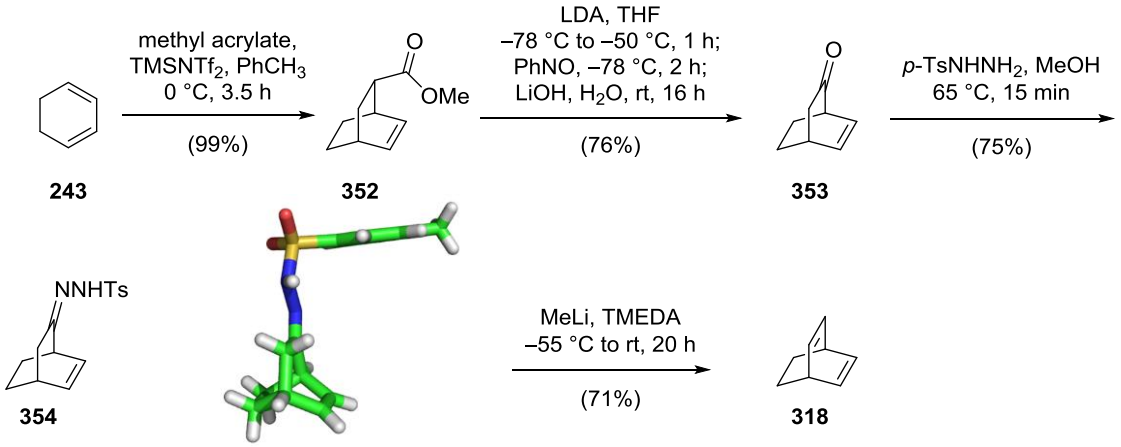
2.3 Precursor Synthesis

In the preceding Master thesis,[148] synthetic work was conducted to establish a reliable route to the precursors of the planned key electrophilic addition. However, it was found that the pursued access to dihydrobarrelene (**318**) employing acetylene equivalent **349** suffered from two issues (Scheme 66).[149] First, the Diels-Alder reaction providing bicyclo[2.2.2]octadiene **350** required very long reaction times and second, the liberation of the double bond after reduction to bicycle **351** provided dihydrobarrelene (**318**) in unsatisfactory yields.



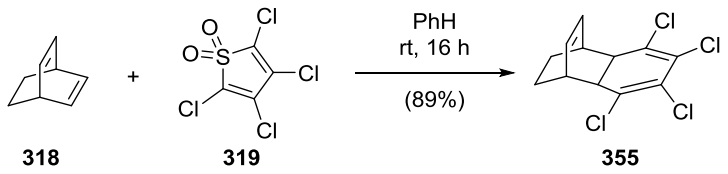
Scheme 66. Previous synthetic route to dihydrobarrelene (**318**).

Since larger quantities of dihydrobarrelene (**318**) were required, an alternative route to the target molecule using more recent methodology was investigated. Thus, in a Lewis acid catalyzed Diels-Alder reaction of cyclohexadiene (**243**) with methyl acrylate bicyclo[2.2.2]octeneester **352** was obtained in excellent yield (Scheme 67).[150],[151] Conversion to ketone **353** using Yamamoto's oxidative dehomologation method proceeded smoothly[152] and a subsequent Shapiro olefination of hydrazone **354** then afforded dihydrobarrelene (**318**) on a reproducible half-gram scale.[153]



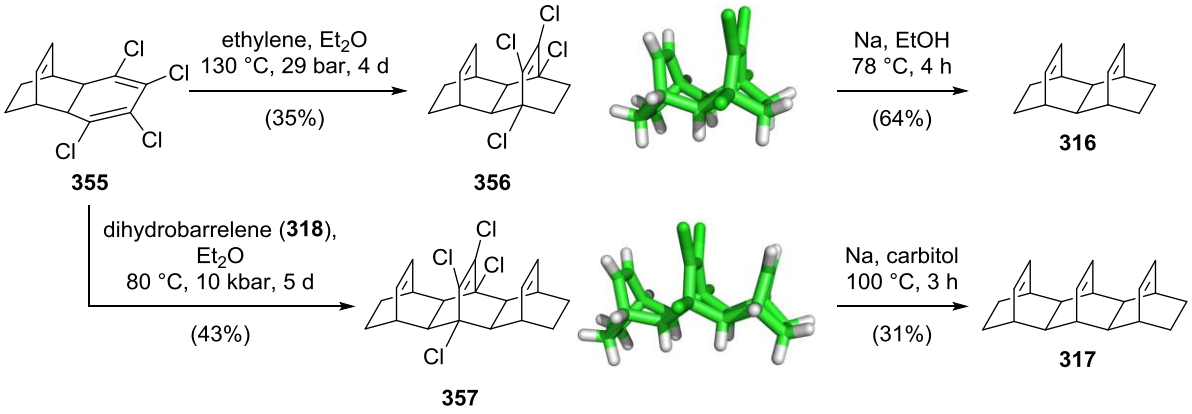
Scheme 67. Efficient route to dihydrobarrelene (**318**) by way of C-C bond cleavage and Shapiro olefination.

The following steps to furnish precursors **316** and **317** were carried out according to the procedure developed by Gleiter and coworkers.[141] Thus, dihydrobarrelene (**318**) was added to thiophene dioxide **319** in a Diels-Alder / cheletropic extrusion cascade leading to triene **355** (Scheme 68).



Scheme 68. Synthesis of triene **355** as a branching point in the synthesis of diene **316** and triene **317**.

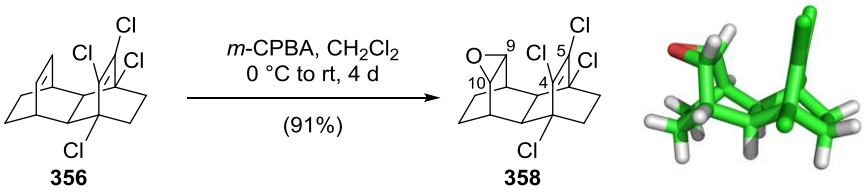
Ethylene was added in a Diels-Alder reaction to triene **355** to give diene **356** which was then dechlorinated to diene **316** (Scheme 69). Respectively, a high pressure Diels Alder reaction of dihydrobarrelene (**318**) to triene **355** yielded hexacyclic triene **357**, the dechlorination of which afforded the desired laticyclic conjugated triene **317**. From chlorinated diene **356** and chlorinated triene **357** crystals suitable for single crystal X-ray diffraction were obtained. Analysis of the X-ray structures showed that the double bonds of diene **356** and triene **357** are spaced by d = 3.0 Å, which is a value significantly below the added van der Waals radii of two carbon atoms (r_C = 1.7 Å).[154] This close proximity of the double bonds leads to the electronic interaction known as the so-called laticyclic homoconjugation.



Scheme 69. Synthesis of the laticyclic conjugated precursors.

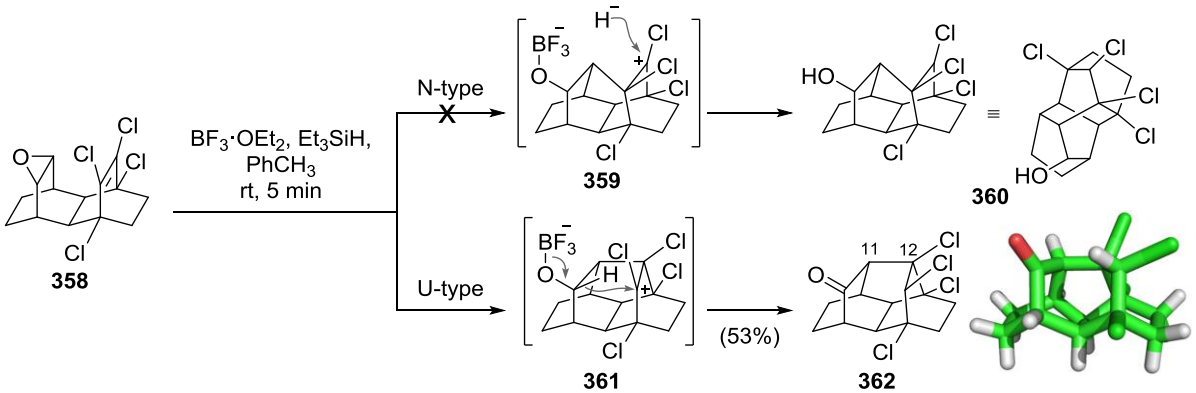
2.4 Synthesis of Tritwistane and Studies toward Hexatwistane

As the dechlorinated model system **326** displayed a higher tendency toward rearrangement reactions, the efforts to synthesize tritwistane **288** were first investigated on chlorinated precursor **356**. Thus, tetrachlorodiene **356** was selectively epoxidized to epoxide **358** (Scheme 70). Analysis of the X-ray structure of epoxide **358** showed that it is approximately C_S-symmetric in the solid state and yielded a C4─C10 (C5─C9) distance of d = 3.0 Å and a C4─C9 (C5─C10) distance of d = 3.3 Å, indicating that the N-type as well as the U-type cyclization are reasonable from a structural point of view.



Scheme 70. Synthesis of epoxide **358** from chlorinated precursor **356**.

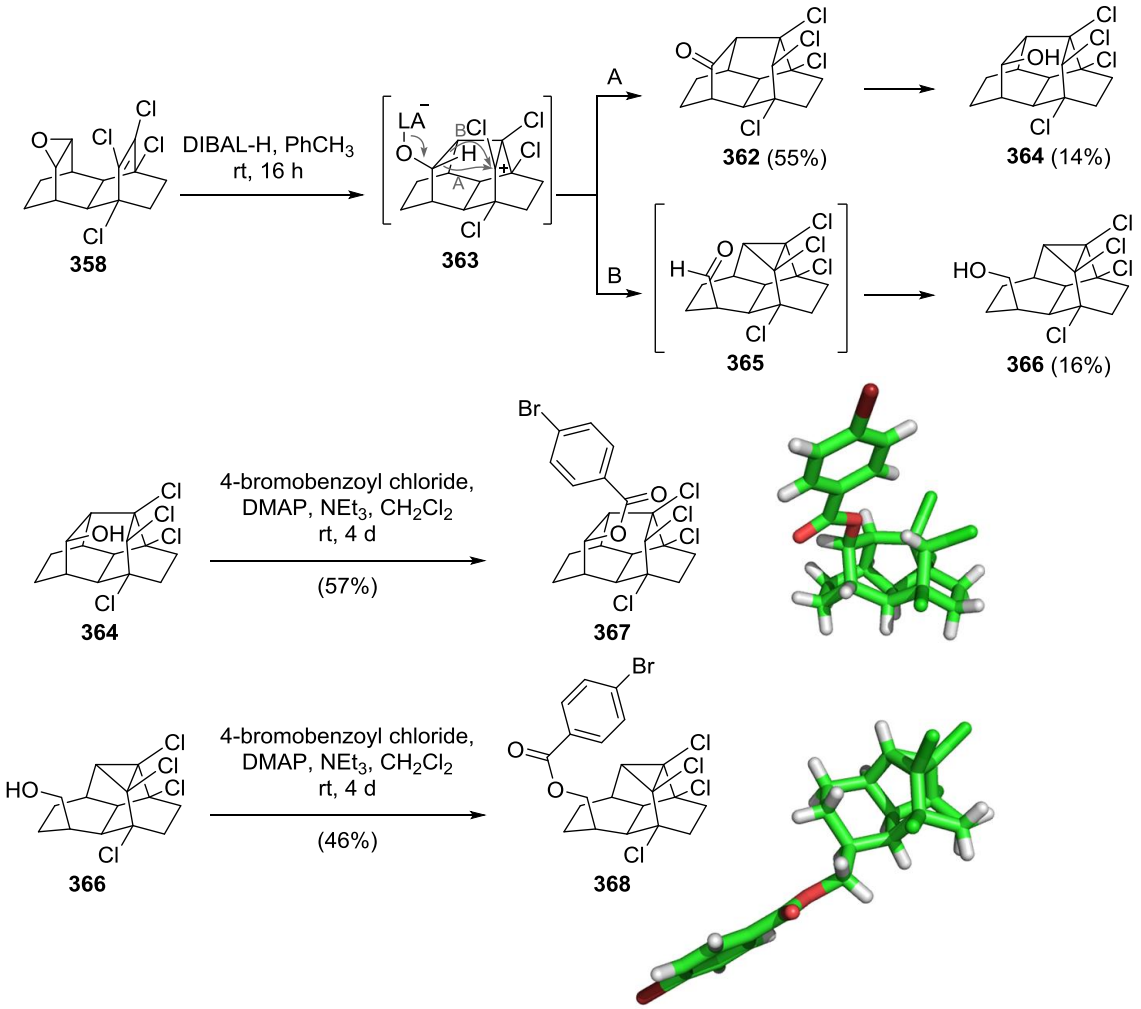
Next, epoxide **358** was to be opened employing a Lewis acid for activation of the epoxide moiety and an external hydride source to allow for the nucleophilic trapping of the generated carbocation. Therefore, envisaged intermediate **359** from an N-type cyclization would give access to tritwistane **360**. As in the case of model system **340**, the only product that was isolated from the reaction mixture was ketone **362** which most likely results from an intramolecular 1,4-hydride shift of U-type cyclized intermediate **361** (Scheme 71). Variation of the reaction conditions to facilitate thermodynamic equilibration did not yield the desired N-type cyclized product **360**. With a bond length of d = 1.59 Å in the crystal structure, the C11─C12 bond in ketone **362** was found to be slightly elongated compared to usual C─C single bonds.[155] This indicates considerable strain in the pentacyclic structure of ketone **362**.



Scheme 71. Conjugate opening of epoxide **358**.

A possible way to enforce the intermolecular delivery of a hydride could be the use of a more reactive hydride source. DIBAL-H was chosen as it is not only a hydride donor but also acts as a Lewis acid. Reacting epoxide **358** with DIBAL-H afforded three species with the major one being ketone **362**

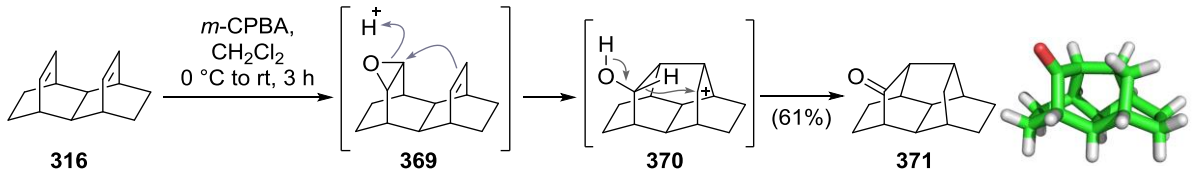
(Scheme 72). Preliminary spectroscopic data established that the other two observed species were alcohols. As a logical consequence of the reductive conditions, structure **364** was assigned by NMR spectroscopy as the alcohol resulting from a reduction from the less hindered face of ketone **362**. More challenging was the structural assignment for the second unknown species, as it displayed a signal for an additional methylene unit in its NMR spectra. In respect to the observations made in the model system, it was proposed that carbocation **363** might be trapped partially in a 1,5-alkyl shift resulting in aldehyde **365**, which would then be reduced under the reaction conditions to primary alcohol **366**. This theory was substantiated as it was found that structure **366** matchs all the spectroscopic data. In the following, the structures of secondary alcohol **364** and primary alcohol **366** were established unambiguously by the conversion to bromobenzoates **367** and **368** and ensuing single crystal X-ray diffraction of suitable crystals. No evidence for N-type cyclizations was found in the system of chlorinated epoxide **358**.



Scheme 72. Conjugate opening of epoxide **358** with the Lewis acidic hydride source DIBAL-H and conversion of the generated alcohols into their bromobenzoates for structural analysis.

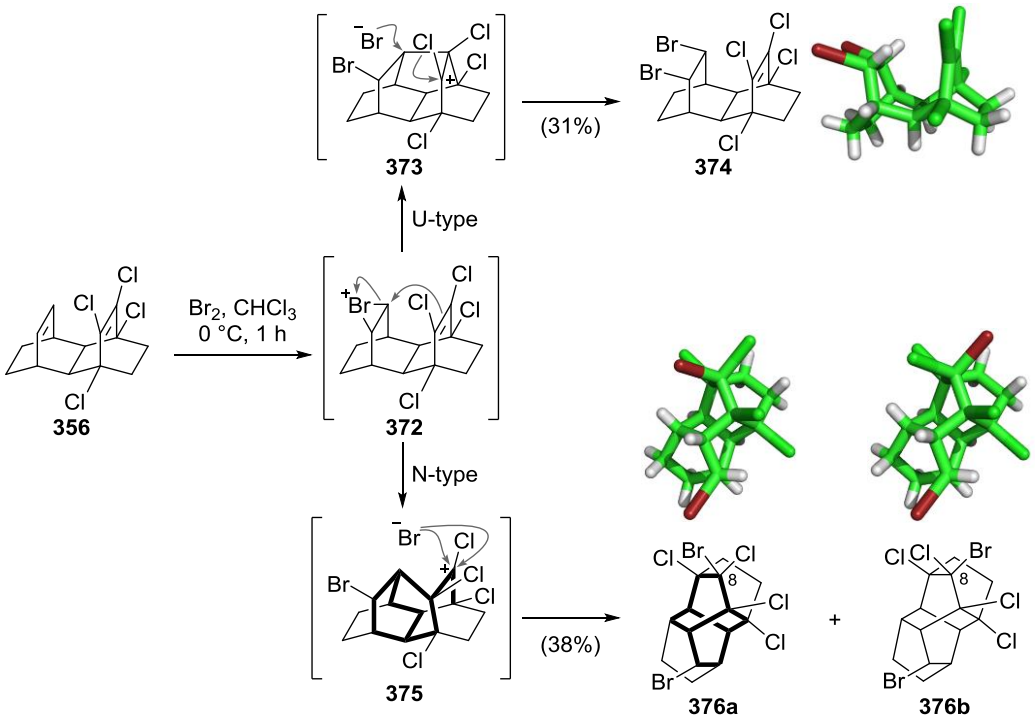
As the reactions in the chlorinated precursor system did not deliver the desired results, the route *via* epoxidation was also applied to dechlorinated precursor **316**. The attempt to effect a monoepoxidation

of diene **316** only resulted in ketone **371**, similar to the previous observations made with model system **326** (Scheme 73). Presumably, intermediately formed epoxide **369** gets protonated by residual acidic species in the reaction mixture, followed by a U-type cyclization leading to pentacyclic carbocation **370**. An ensuing 1,4-hydride shift then affords ketone **371**, which was already observed during studies in the preceding Master thesis but was identified unambiguously for the first time *via* single crystal X-ray diffraction.[148] Despite not providing the products of the desired N-type cyclization, the epoxidation studies on diene system **316** and **356** furnished two new carbocyclic cage structures which were verified by X-ray studies.



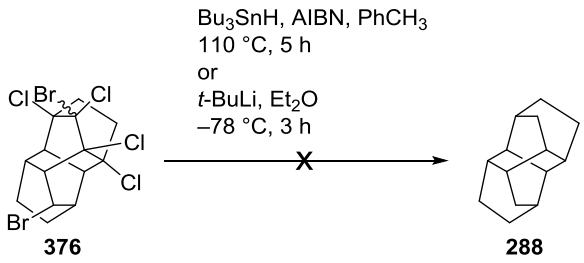
Scheme 73. Attempt to epoxidize precursor **316** resulting in the formation of ketone **371**.

Judging from the results above, it seems that the conjugate opening of epoxides in laticyclic systems **316** and **356** generally proceeds in a U-type cyclization. As a result, a bromination reaction was tested as a second set of electrophilic addition conditions. For the first attempt, chlorinated precursor **356** was chosen due to the presumably lower rearrangement tendency. Thus, the bromination of diene **356** afforded two new species (Scheme 74). One of them displayed only 7 signals in its ^{13}C NMR spectrum indicating a C_s-symmetry for its molecular structure. The additional appearance of one proton resonance corresponding to a bromomethylene unit facilitated assignment of structure **374**. For the second species complicated NMR spectra were obtained which implicated a mixture of two isomers and did not allow the unambiguous identification of the molecular structure. Single crystal X-ray diffraction studies clearly established structures **374** and **376** for the products of the bromination reaction. Presumably, intermediately formed bromonium ion **372** can open in a U-type cyclization to afford carbocation **373** as well as an N-type cyclization resulting in intermediate **375**. Carbocation **373** then gets trapped in a vinylogous S_N2 attack of bromide which affords the regeneration of one double bond and results in the formation of vicinal dibromide **374** under double inversion. In contrast, N-type cyclized intermediate **375** is trapped directly to provide hexahalogenated tritwistane **376**. Apparently the nucleophilic attack on carbocation **375** is viable from both sides as a 7 : 3 mixture of diastereomers at C8 was observed. Since dibromide **376a** was formed as the major diastereomer, the attack from the internal side seems to be favored. It was not possible to separate diastereomers **376a** and **376b** as they co-crystallize and are of equal polarity.



Scheme 74. Bromination of chlorinated precursor **356** resulting in vicinal dibromide **374** and tritwistane **376**.

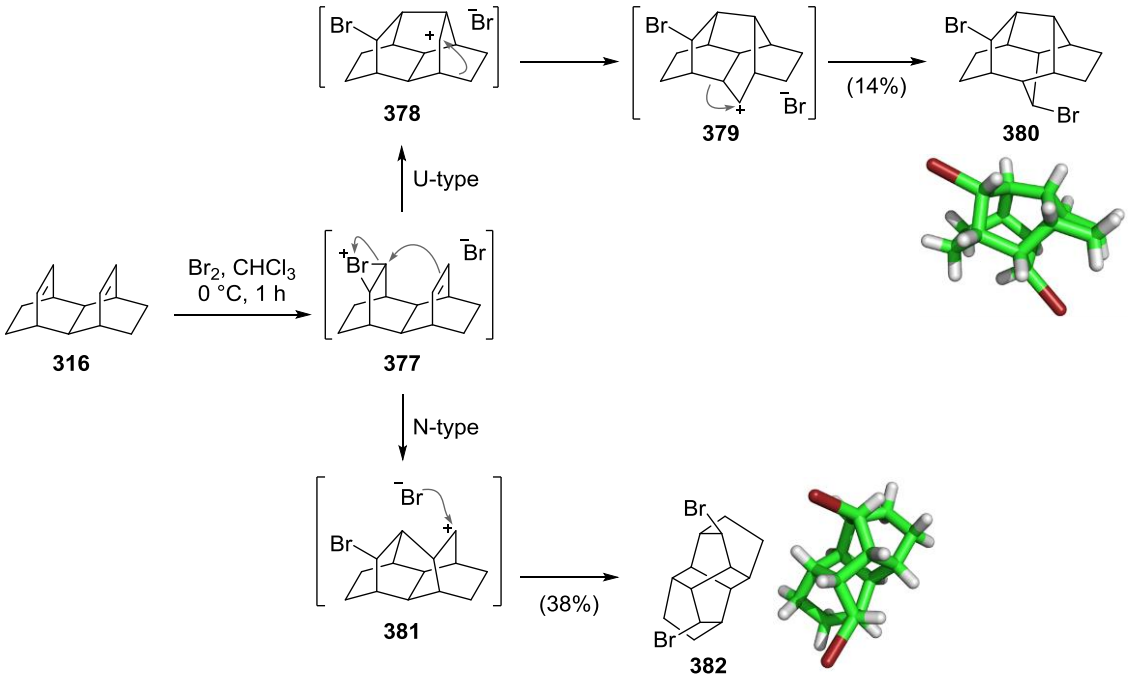
Next, global dehalogenation of hexahalogenated tritwistane **376** was investigated. Radical reductive conditions as well as metalation/protonation conditions failed to deliver the desired tritwistane (**288**) (Scheme 75). A reason for this could be the general difficulty to remove chlorine atoms, which usually requires very harsh conditions as in the dehalogenation of diene **356**. These conditions would highly likely lead to elimination reactions in system **376**.



Scheme 75. Futile attempts to defunctionalize hexahalogenated tritwistane **376**.

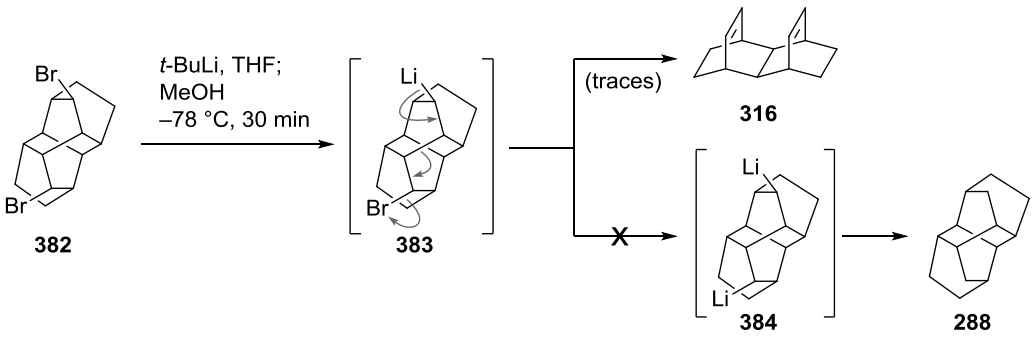
Encouraged by the formation of the tritwistane skeleton in the bromination of diene **356** we turned to dehalogenated precursor **316**. This precursor should, in case of a successful bromination reaction, allow the dehalogenation more easily, as bromine atoms can generally be removed under milder conditions. From the bromination reaction of precursor **316** two products were isolated (Scheme 76). Structural assignment based on NMR spectroscopy proved difficult as both compounds displayed 14 signals in their ^{13}C NMR spectrum indicating C_1-symmetry in the structures. Unambiguous identification was made possible by single crystal X-ray diffraction studies. Therefore, the structures of dibromide **380** and dibromotritwistane **382** were assigned to the products. Dibromide **380**

presumably is formed after U-type cyclization of intermediate bromonium ion **377** in a sequence of two Wagner-Meerwein rearrangements *via* carbocations **378** and **379** and a face-selective trapping by bromide. In contrast, dibromotritwistane **382** results from an N-type cyclization of bromonium ion **377** and a nucleophilic attack on intermediately formed **381** selectively from the internal face. In light of the diastereomeric mixture observed for hexahalogenated tritwistane **376** this selectivity is quite remarkable.



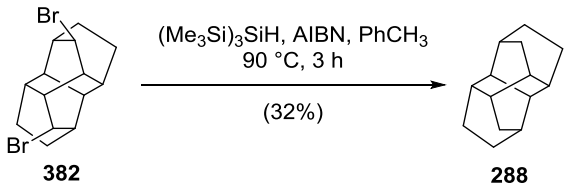
Scheme 76. Synthesis of dibromotritwistane **382** by bromination of precursor **316**.

In order to access the desired parent hydrocarbon tritwistane (**288**), dehalogenation was investigated next. The first attempt using metalation/protonation conditions afforded only precursor **316** (Scheme 77). This observation can be explained by a Grob elimination of LiBr from monolithiated intermediate **383**. Seemingly, this course of the reaction occurs faster than a second lithiation to dilithiated species **384** which would, after quenching, yield the desired tritwistane (**288**). None of the desired material could be identified in the reaction mixture.



Scheme 77. Attempt to dehalogenate **382** under metalation/protonation conditions resulting in precursor **316**.

As a consequence, dibromotritwistane **382** was to be submitted to reductive radical conditions to facilitate selective dehalogenation avoiding elimination reactions. Indeed, heating **382** with Chatgilialoglu's reagent as hydrogen radical donor in toluene in the presence of AIBN afforded tritwistane (**288**) (Scheme 78).[156] However, the desired product was contaminated with a silane species, which could not be removed by column chromatography. Prolonged stirring of a solution of this mixture with polymer supported fluoride finally afforded pure tritwistane (**288**) as a colorless, waxy and volatile solid.



Scheme 78. Dehalogenation of dibromotwistane **382** using reductive radical conditions.

The formation of tritwistane (**288**) is evident from its simplified ^{13}C spectrum compared to the spectroscopic data of its precursor (Figure 10). Whereas C_1-symmetric dibromotritwistane **382** displays 14 signals, tritwistane (**288**) contains only 7 magnetically unequivalent carbon atoms due to its C_2-symmetry and thus only shows 7 resonances. For the spectral identification of potential polytwistane (**85**) (Chapter 3) the central methine unit of tritwistane (**288**) is of vital importance. This methine has the largest distance from the termini and is only surrounded by other methines, similarly to the environment in the ideal polymer. Analysis of the NMR spectra of tritwistane (**288**) affords a ^{1}H NMR shift of δ = 1.48 ppm and a ^{13}C NMR shift of δ = 35.4 ppm for this central methine unit. Both values are in the common range for a trisubstituted carbon unit, indicating that there is no extraordinary amount of strain present in the structure as compared to for example cubane (**10**).[157] The combination of both values might give a first hint as to where the NMR signals of polytwistane can be expected.

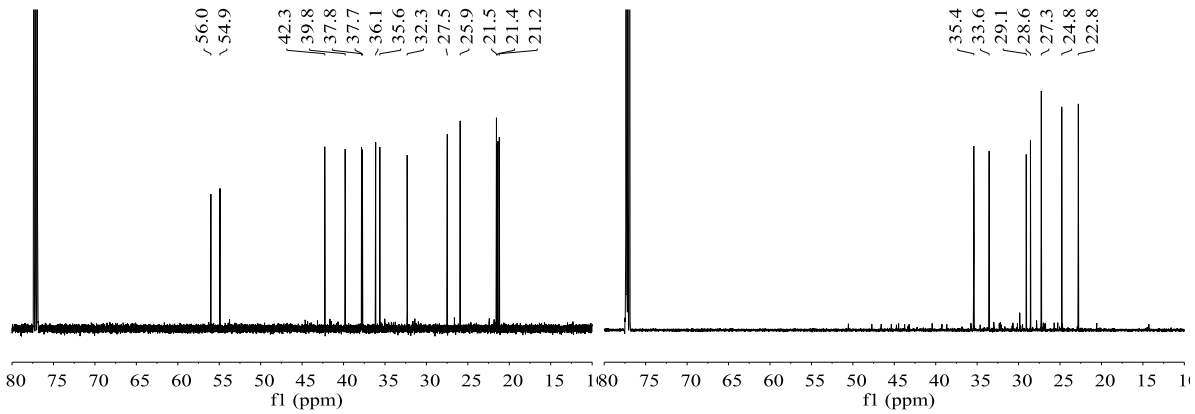
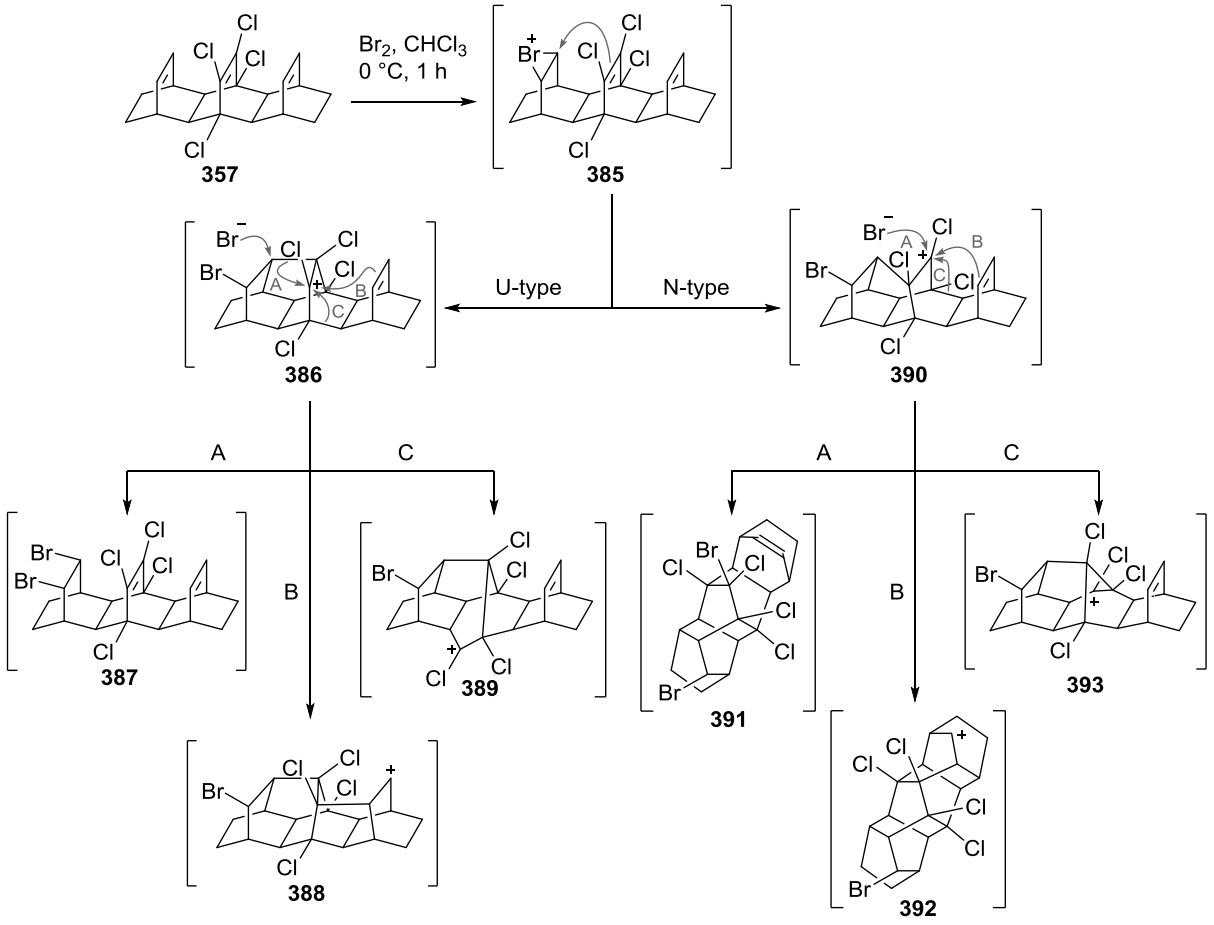


Figure 10. Relevant section of the ^{13}C NMR spectra of dibromide **382** (left) and C_2-tritwistane (**288**) (right).

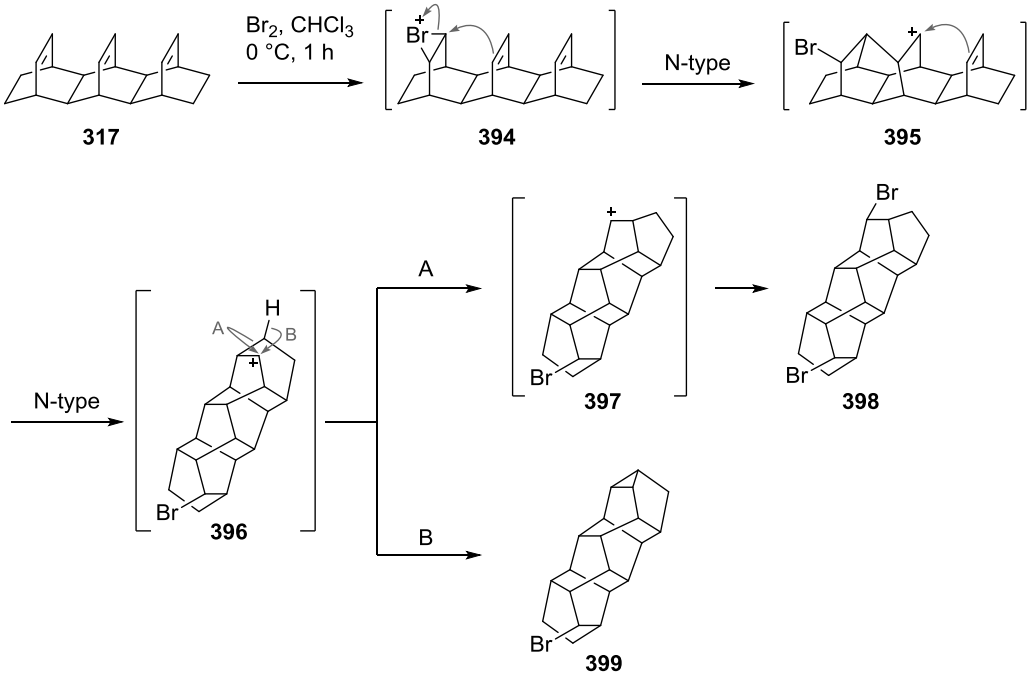
After the successful synthesis of tritwistane (**288**) the next objective was to synthesize hexatwistane (**291**) starting from precursors **317** and **357**. Based on the insights from the synthesis of tritwistane (**288**) it was decided to use bromination conditions for this purpose. First attempts were carried out on the chlorinated derivative as the dechlorination of **357** yielded **317** only in moderate yields thereby limiting its availability. Thus, tetrachlorotriene **357** was submitted to bromination at T = 0 °C resulting in the formation of a complex mixture of brominated products according to mass spectrometry. The multitude of products can be explained with the variety of possible rearrangement pathways (Scheme 79). Accordingly, intermediately formed bromonium ion **385** can interact with the neighboring double bond in two ways, namely a U-type cyclization or an N-type cyclization. Intermediate **386** from the facultative U-type cyclization then can react further in several ways including nucleophilic trapping, interaction with the next double bond or Wagner-Meerwein rearrangements, possible products of which would be dibromide **387** and carbocations **388** and **389**, respectively. The same holds true in case of N-cyclized intermediate **390** which could give rise to **391**, **392** and **393**. Beyond this, the generated carbocations **388**, **389**, **391** and **392** can further rearrange and therefore generate a complex mixture.



Scheme 79. Selection of possible paths in the bromination of **357**. A = nucleophilic trap. B = laticyclic interaction. C = Wagner-Meerwein rearrangement.

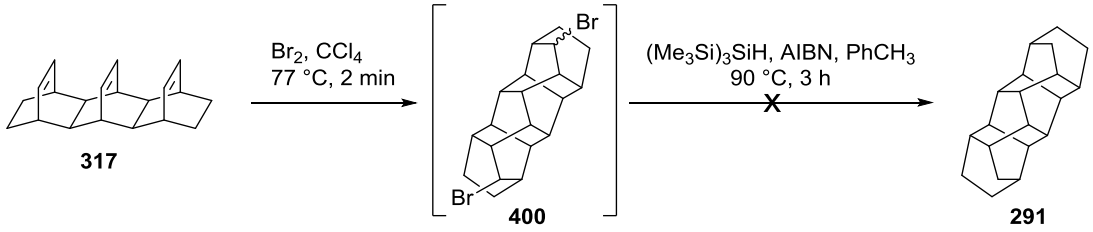
Due to the expected almost identical polarity of the products, column chromatography is not likely to be effective for the purification of the reaction mixture. Indeed, the purification of the obtained crude mixture by column chromatography was not successful. Recrystallization from different solvent systems also proved futile and did not provide crystals suitable for single crystal X-ray diffraction. As a result, no structures could be assigned to the reaction products.

Consequently, the bromination of dehalogenated triene **317** was investigated. The result was again a complex mixture, which was unfortunately inseparable by column chromatography. However in this case, recrystallization from hexanes afforded crystals that seemed suitable for single crystal X-ray diffraction. Upon analysis, it turned out that the crystal was highly disordered therefore not allowing a satisfying elucidation of the structure. A second crystal did not provide any better results. Preliminary results from structure analysis showed two species which might be present in the crystal, dibromide **398** and cyclopropane **399** (Scheme 80). This result indicates that indeed the desired double N-type cyclization of bromonium ion **394** might have occurred, *via* carbocation **395**. The generated hexatwistane carbocation **396** then in one case underwent a Wagner-Meerwein rearrangement to **397** which was trapped by bromide resulting in dibromide **398** and in the other case was cornerstone deprotonated affording cyclopropane **399**. As the sites of the bromine atoms as well as the carbon scaffold are only partially occupied in the crystal, this structural analysis is not reliable. Nevertheless it can be assumed that these species are at least to some extent present in the reaction mixture.



Scheme 80. Presumable results from the bromination of laticyclic triene **317**. A = Wagner-Meerwein rearrangement. B = cornerstone deprotonation.

Following reports by the groups of Balci and Dastan, the bromination of laticyclic triene **317** was also conducted under high-temperature conditions in order to avoid rearranged products.[158] As before only complex reaction mixtures were obtained. Since the formation of the desired dibromohexatwistane **400** cannot be ruled out on these grounds, it was tried to dehalogenate the crude reaction mixture from the bromination reaction (Scheme 81). No material which might correspond to the desired hexatwistane (**291**) was obtained.

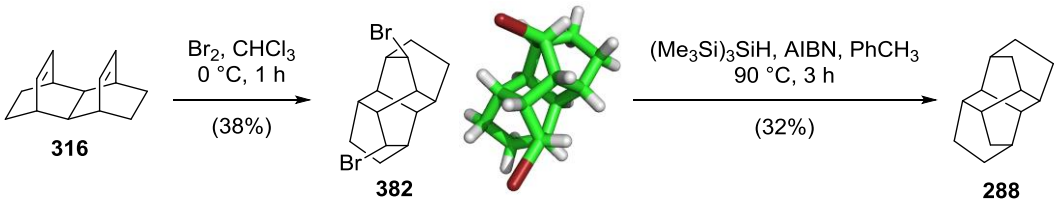


Scheme 81. Effort to avoid rearranged products by high-temperature bromination.

The huge variety of possible side reactions (as indicated in Scheme 79) and the same polarity of the products renders the isolation and purification of the desired hexatwistane (**291**) impossible, if it is formed at all. In addition to this, the procurement of the cyclization precursors is difficult because of high-pressure reactions and low-yielding dehalogenation steps. Therefore, the N-type cyclization of extended laticyclic oligoenes does not seem suitable for the synthesis of polytwistane (**85**). Strategies to obtain this polymer by other methods are addressed in the next chapter.

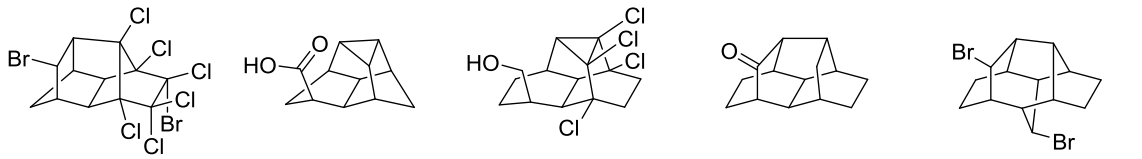
2.5 Conclusion and Future Directions

In this part of the thesis, the synthesis of C_2-symmetric tritwistane (**288**) was achieved. The synthesis was performed *via* bromination of a suitable laticyclic diene precursor **316**, which was available in seven steps from cyclohexadiene (**243**) (Scheme 82). The structure of dibromotwistane **382** was unambiguously proven by single crystal X-ray diffraction and was dehalogenated successfully using radical conditions. Spectroscopic analysis afforded a ^{1}H NMR shift of δ = 1.48 ppm and a ^{13}C NMR shift of δ = 35.4 ppm for the central methine unit of C_2-tritwistane (**288**). This spectroscopic data is of interest for the identification of polytwistane (**85**) by NMR spectroscopy.



Scheme 82. Successful synthesis of C_2-tritwistane (**288**).

During these studies several interesting rearrangements were observed which led to the identification of new carbocyclic cage compounds. Thus, the previously proposed bromination product of isodrine (**325**) was reassigned to dibromide **339** (Figure 11). Cyclopropanes **348** and **366** were found as a result of an interesting 1,5-alkyl shift, whereas ketone **371** was formed by a hydride shift, which is precedented in the isodrine system. Finally, dibromide **380** arose from a double Wagner-Meerwein rearrangement. Beside their aesthetic appeal, these structures may help in the understanding of similar processes in more complex settings.



339 [6.4.0.0^{2,10}.0^{3,7}.0^{5,9}] **348** [6.3.0.0^{2,4}.0^{3,7}.0^{5,9}] **366** [7.4.0.0^{2,4}.0^{3,8}.0^{5,10}] **371** [7.4.1.0^{4,12}.0^{5,14}.0^{6,11}] **380** [7.5.0.0^{2,12}.0^{3,8}.0^{5,11}]

Figure 11. Rearranged products displaying new carbocyclic cages with the numbering of the pentacyclic systems according to IUPAC.

Investigation toward C_2-symmetric hexatwistane (**291**) using the same reaction conditions resulted only in complex mixtures. Preliminary crystallographic data of a highly disordered crystal established a high probability of undesired side products. While it is possible that the desired hexatwistane scaffold occurs in the reaction mixture, this result indicates that the electrophilic addition method is not suitable for the synthesis of higher oligotwistanes or polytwistane (**85**) due to highly divergent rearrangement pathways.

3 Synthetic and Theoretical Studies toward Polytwistane

3.1 Background and Aims

As previously outlined (Scheme 56), the linear extension of twistane (**254**) with ethano bridges leads, *via* oligomers like hexatwistane (**291**), nonatwistane (**294**), dodecatwistane (**401**), pentadecatwistane (**402**) or hexadecatwistane (**403**), ultimately to polytwistane (**85**) (Figure 12). Due to its construction from twistane (**254**), polytwistane (**85**) retains the D_2-symmetric twist-boat conformation in all constituting cyclohexane rings and as a result displays helical chirality. Additional features are that polytwistane (**85**) contains hydrogen atoms and sp^3 hybridized carbon atoms that all possess the same chemical environment. Therefore the ideal polymer is expected to exhibit one single resonance in ^1H and ^{13}C NMR, respectively. Ideal polytwistane (**85**) is a structural isomer of polyacetylene and therefore has the same molecular formula $(C_2H_2)_n$ but in contrast is fully saturated. The inner and outer diameter of polytwistane (**85**) amount to D_i = 2.6 Å and D_o = 4.7 Å, which would render it the smallest carbon nanotube to date.[159] Using computational chemistry it was shown that a polymerization of acetylene to polytwistane (**85**) is highly exothermic.[46]

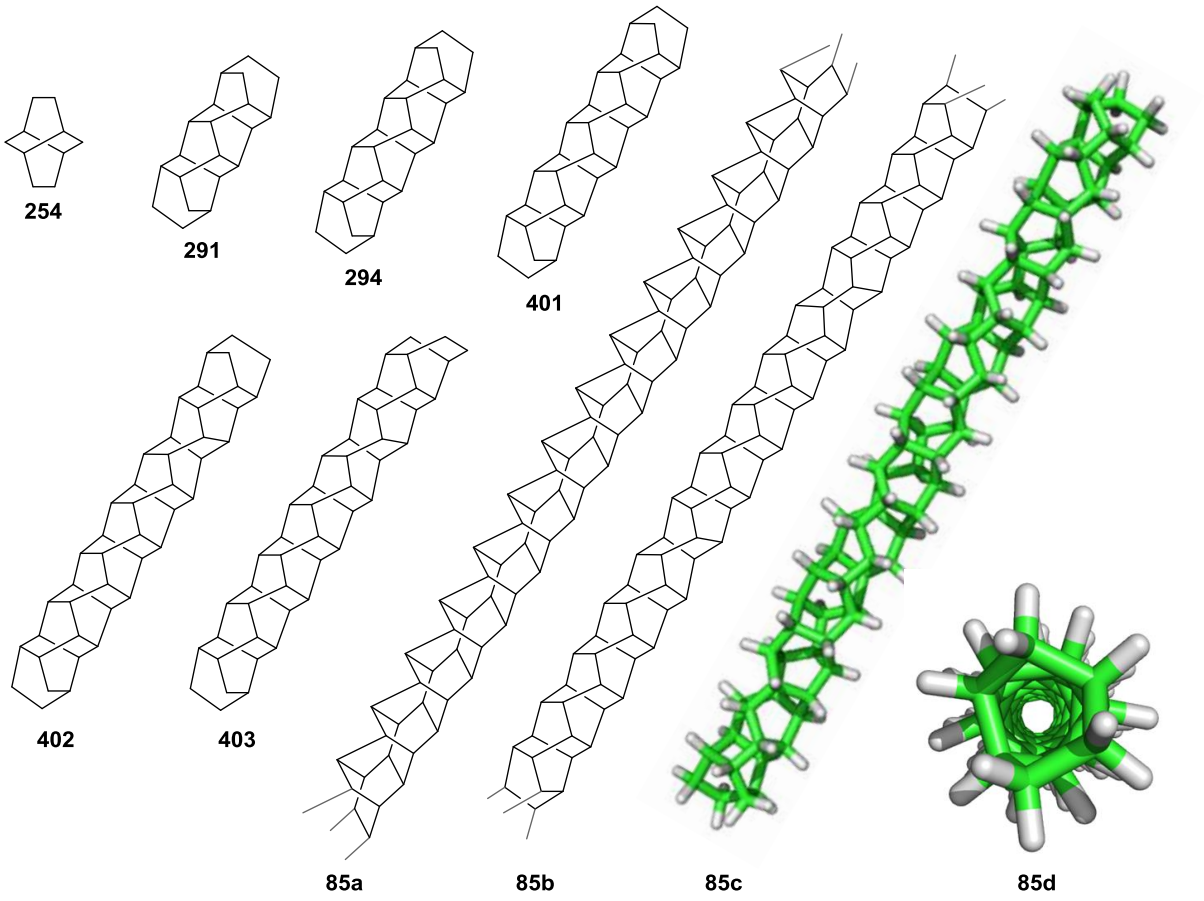


Figure 12. Structures of twistane (**254**) and oligotwistanes. Structure of polytwistane (**85**): drawing emphasizing the relationship to bicyclo[2.2.2]octane (**85a**), drawing emphasizing the structural unit of twistane (**85b**), side view (**85c**) and top view (**85d**) of a $C_{86}H_{92}$ fragment of polytwistane optimized at the B3LYP/6-31G(d) level.[192]

Due to its structure and composition, polytwistane (**85**) can be contemplated as a fully hydrogenated chiral CNT. This relationship is similar to that between graphane and graphene with the difference being that the hydrogenation of graphene has to occur from two faces while CNTs are hydrogenated only from one face.[49,104]

CNTs are classified into three classes: armchair (*n*,*n*)-CNTs, with the basic building block being cycloparaphenylenes (**404**), zig-zag (*n*,0)-CNTs, with the building block being cycloacenes (**408**) and chiral (*n*,*m*)-CNTs with the building block being acene-inserted cycloparaphenylenes (**412**) (Figure 13).[109] Regarding the very small diameter of polytwistane (**85**) previous reports on ultrasmall CNTs are of special interest for setting polytwistane into context with CNTs.[159] The smallest CNT known to date, (*2*,*2*)-CNT (**405**) is an armchair CNT and its formation was observed inside a multi-walled CNT as well as in a zeolite.[159a,b] Its smallest structural unit, [2]-cycloparaphenylene (**406**), is hitherto experimentally unrealized. The hydrogenation of **405** and its corresponding fully hydrogenated structure (**84**) were studied theoretically, but no sophisticated attempts to synthesize from defined precursors have been reported yet.[45,160] In contrast, the synthesis of the smallest unit of the fully hydrogenated CNT **84**, tricyclic hydrocarbon **407**, was reported by Eaton and Chakraborty in 1978.[161]

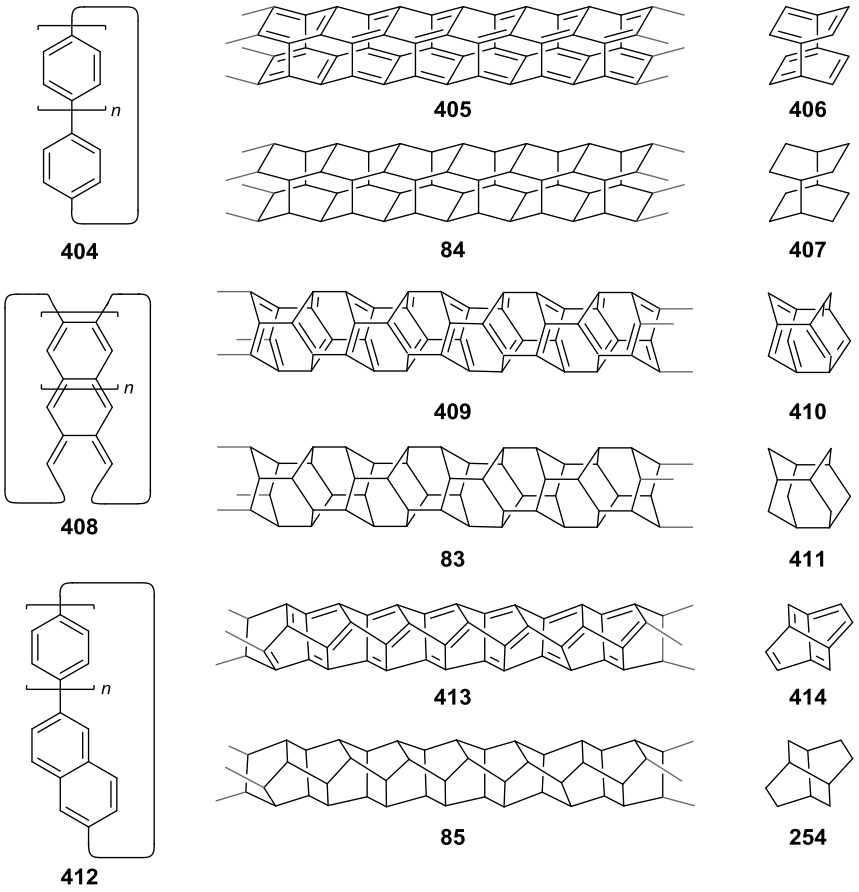
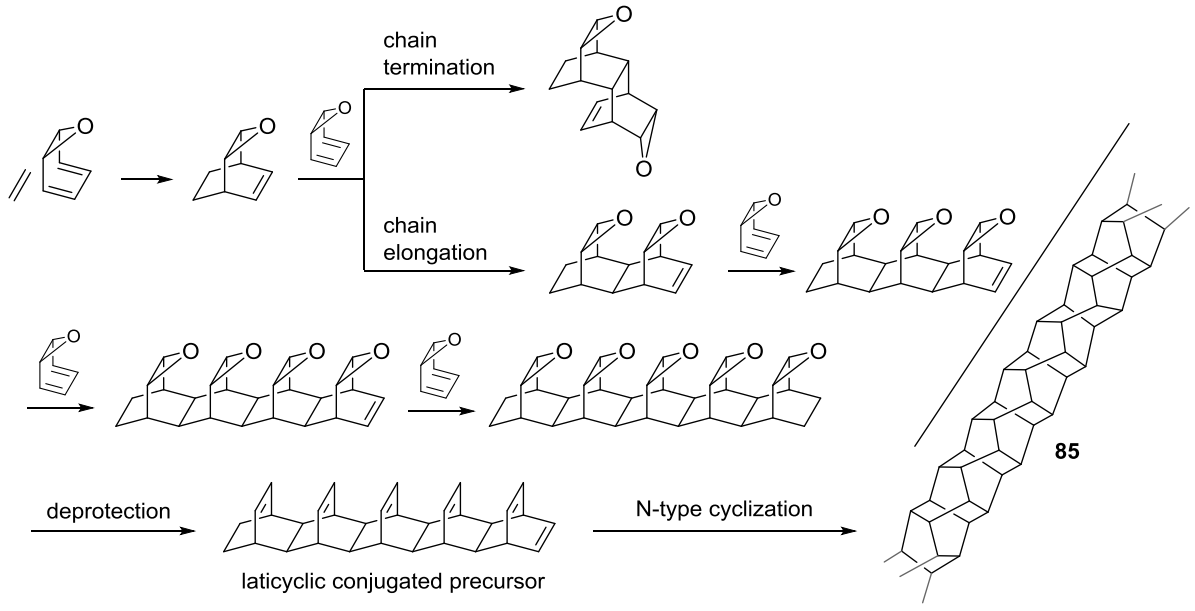


Figure 13. Generic building blocks of the three types of CNTs (**404**, **408** and **412**) with *n* defining the width of the respective CNT, the corresponding smallest possible CNTs of these types (**405**, **409**, **413**), their fully hydrogenated derivatives (**84**, **83**, **85**) and the respective structural units.

Vice versa, the smallest possible zig-zag CNT would be (*3,0*)-CNT (**409**) but as yet this structure has not been observed experimentally just as the constituting unit [3]-cycloacene (**410**).[162] Again, the related hydrogenated structure **83** was examined theoretically but was never observed in the laboratory.[45] In contrast, the structural unit of **83** was synthesized by several groups and termed iceane (**411**).[163] The smallest possible CNT belonging to the class of chiral CNTs would be (*2,1*)-CNT (**413**). This structure is also not precedented in the literature and the structural unit, tricycle **414**, is likewise unknown. The complete hydrogenation of this CNT would lead to the structure of polytwistane (**85**) which was for the first time considered during the current work.

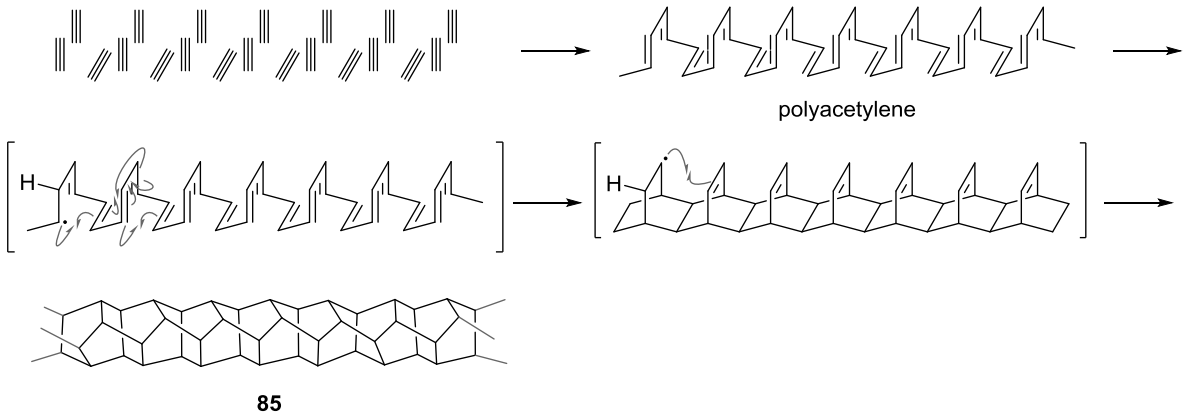
The hydrogenation of single-walled CNTs is a current topic of investigation in order to establish CNTs as a material for hydrogen storage. This is a result of previous attempts using physisorption of hydrogen to CNTs for the same purpose, which gave only unsatisfactory results.[164] Although the hydrogenation studies showed that a partial hydrogenation of single-walled CNTs was possible, complete conversion was not achieved and the products were not structurally characterized.[165] Thus, it seems that a more rational approach is necessary to access these hydrocarbon polymers selectively.

For the synthesis of polytwistane (**85**) several strategies with differing degrees of assumed feasibility were designed within this project. The first strategy features a Diels-Alder reaction of a benzene equivalent, like benzene oxide,[166] with ethylene followed by a sequence of Diels-Alder additions of the benzene equivalent to the growing chain (Scheme 83). This poly-Diels-Alder reaction would after appropriate liberation of the unsaturated moieties result in a laticyclic conjugated precursor. This could then, in an N-type cyclization, be converted to polytwistane (**85**). Aside from the problematic facial selectivity of the Diels-Alder reaction which would likely result in chain termination after the second addition, the studies in the preceding chapter suggested that the cyclization step would most probably not give the desired N-type cyclized product, at least under electrophilic addition conditions.



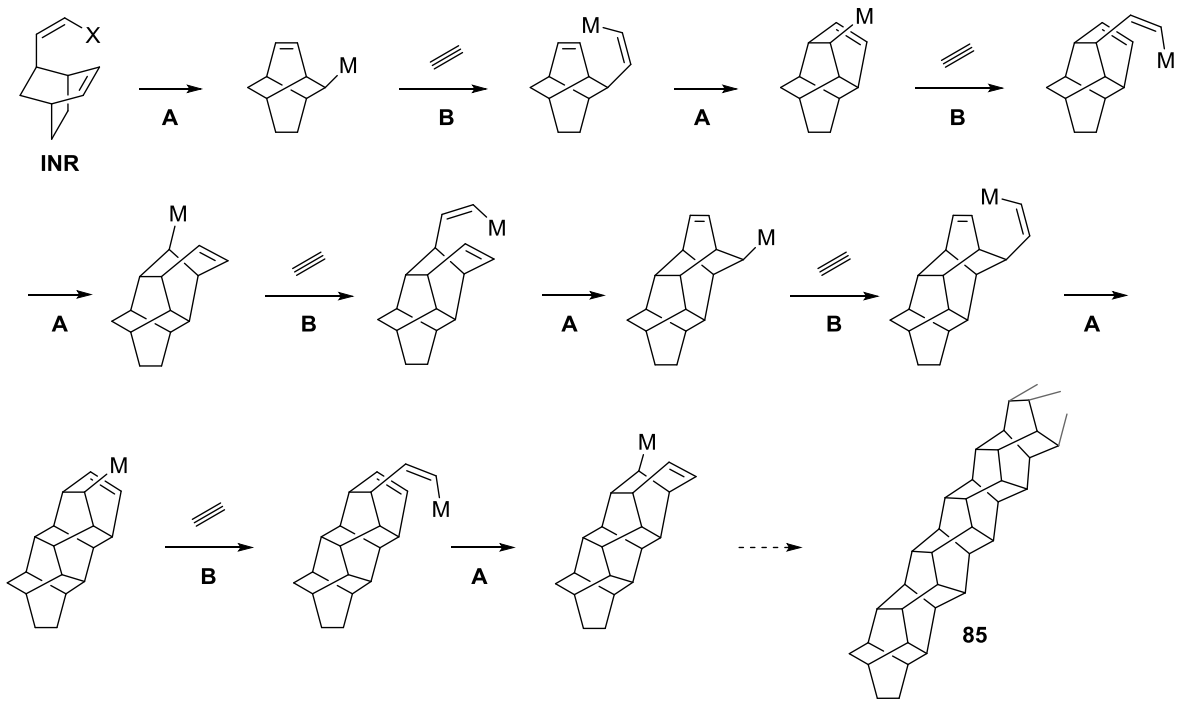
Scheme 83. Proposed synthesis of polytwistane (**85**) by a Diels-Alder polymerization / N-type cyclization.

Another possible synthesis starts with the polymerization of acetylene (Scheme 84).[167] The formed polyacetylene could then in a two-staged radical olefin polymerization be transformed to the desired polytwistane (**85**). Several forms of polyacetylene have been reported, some of which might be particularly interesting for the envisioned radical polymerization. Thus, a possible pre-organization of the polymer, like in helical polyacetylene, might help to bias the polymerization to the desired scaffold.[168] Indeed, an arguable case of an acetylene polymerization exists in the literature where partially saturated species were observed in the product of the polymerization, which possibly could even be polytwistane (**85**).[169] Although the second stage of the planned polymerization would have to occur *via* an N-type cyclization, this pathway might still be possible by thermodynamic equilibration of the cyclization under radical conditions.

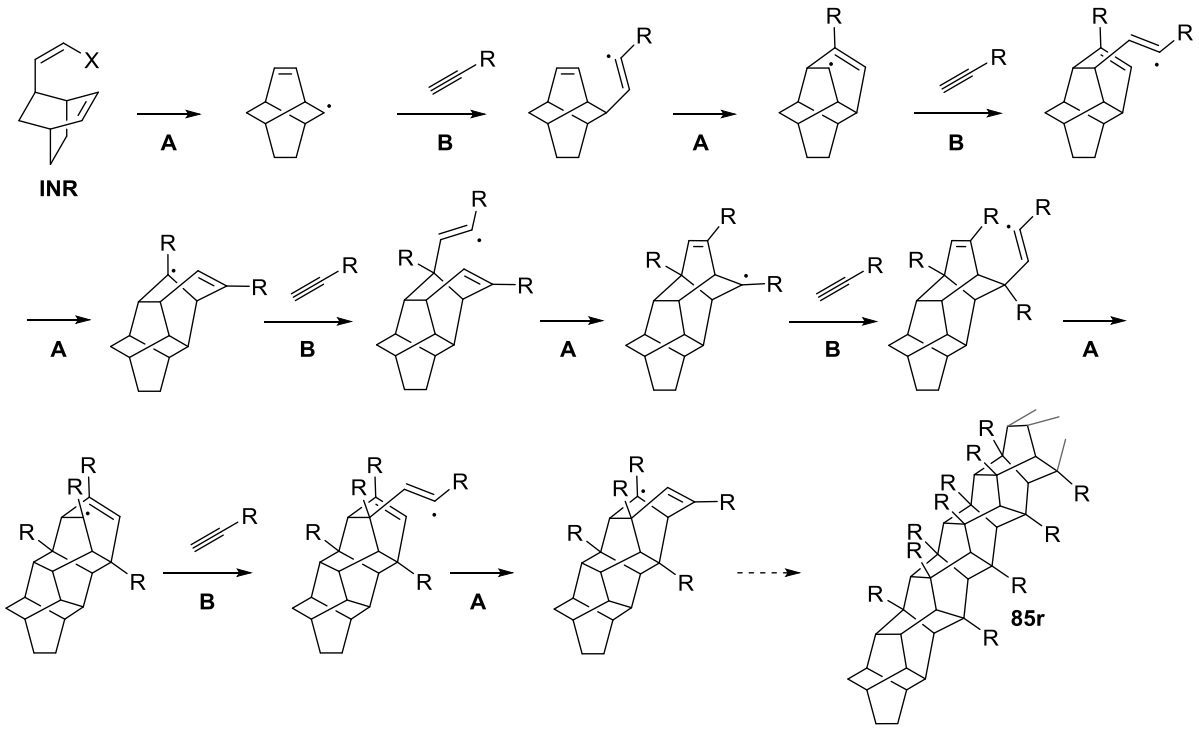


Scheme 84. Proposed synthesis of polytwistane (**85**) by a radical polymerization of polyacetylene.

A conceptually different strategy is the initiator-biased polymerization of acetylene. This approach is based on a bicyclic initiator compound **INR** which contains cyclohexane rings in the boat conformation, in order to bias the polymerization toward the desired twist-boat scaffold (Scheme 85). The first step of a transition metal-catalyzed polymerization would then be the oxidative addition of the transition metal to the alkenyl halide functionality of the initiator **INR**. In a subsequent intramolecular carbometalation step (**A**), a 6-membered ring would be formed, thereby generating an alkyl transition metal complex. This cyclization step is decisive for the outcome of the polymerization as the desired 6-*endo*-*trig* mode has to compete against an unwanted 5-*exo*-*trig* mode, due to the bicyclic structure of the initiator compound **INR**. As there are two carbocycles formed in this cyclization step, the 6-*endo*-*trig* mode can be also considered as 6-*exo*-*trig* mode and the 5-*exo*-*trig* cyclization is at the same time a 7-*endo*-*trig* cyclization. The described intramolecular carbometalation would in the next step be followed by an intermolecular carbometalation to acetylene (**B**) resulting in an alkenyl palladium complex. Subsequent alternating intra- (**A**) and intermolecular (**B**) reactions would then ultimately result in polytwistane (**85**).



Scheme 85. Proposed synthesis of polytwistane (**85**) in an initiator biased transition metal-catalyzed acetylene polymerization. **A** = intramolecular carbometalation (6-*endo*-*trig*). **B** = intermolecular carbometalation to acetylene. M = metal; X = Br, I.

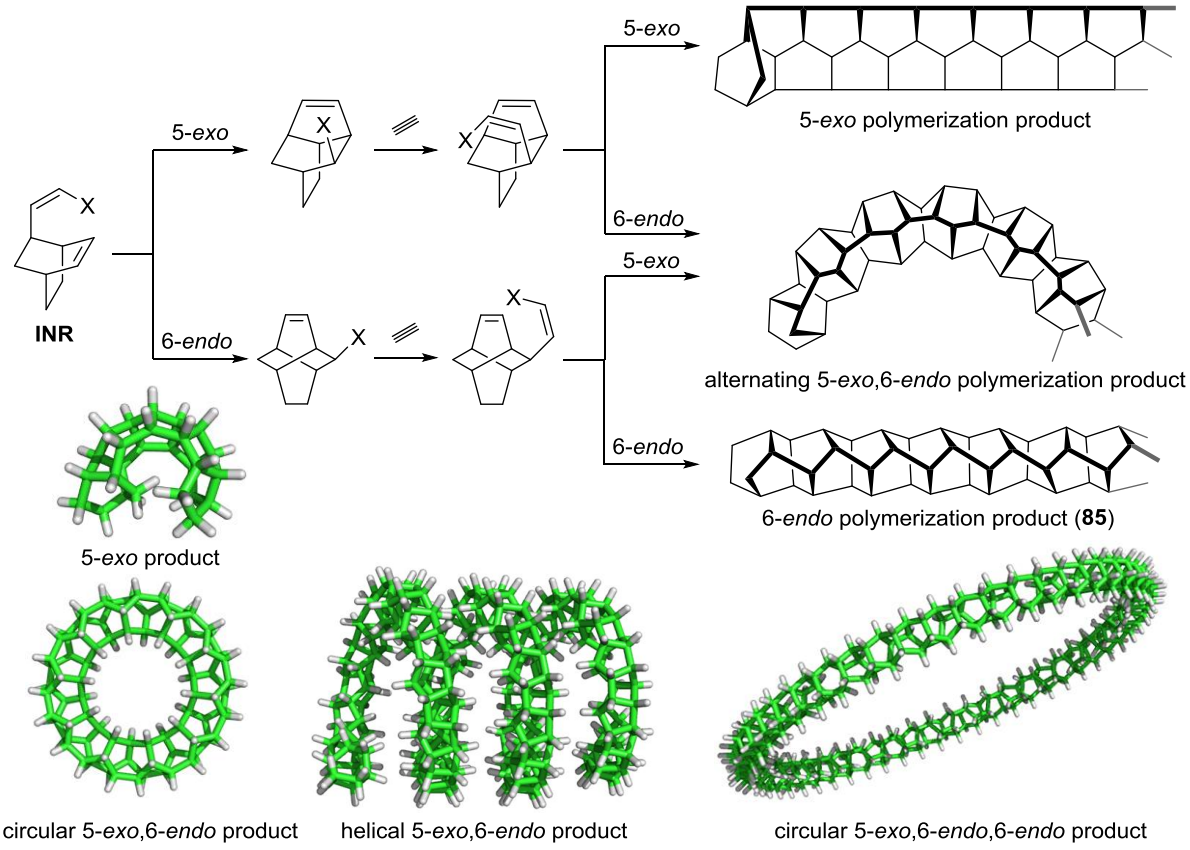


Scheme 86. Proposed synthesis of polytwistane (**85**) in an initiator-biased radical acetylene polymerization. **A** = radical cyclization. **B** = radical addition to acetylene. X = Br, I; R = H, Me, Bu, *n*-Hex, CO_2Me, Ph, CN.

The concept of an initiator-biased acetylene polymerization is also possible using radical conditions. In this case, the alkenyl halide functionality of the initiator **INR** would be cleaved homolytically (Scheme 86). The resulting alkenyl radical would then undergo radical cyclization (**A**) forming a

6-membered ring and a secondary alkyl radical. This would then add in the next step to acetylene (R = H) to afford again an alkenyl radical (**B**). Iterative alternation of these steps would eventually result in the formation of polytwistane (**85**). Also, a radical polymerization employing mono-substituted acetylenes is conceivable for the synthesis of substituted polytwistanes (R ≠ H). The variation of the substituent would give the opportunity to affect the physical properties of the polymer for example by the introduction of solubility enhancing alkyl chains (R = Me, Bu, *n*-Hex). Additionally, radical stabilizing groups (R = CO_2Me, Ph, CN) might facilitate the desired cyclization mode and thus enforce the formation of the polytwistane scaffold.

As previously outlined, the regioselectivity of the cyclization step (**A**) is crucial for the outcome of the polymerization. The initiator compound **INR** is planned to exert the structural bias toward the desired 6-*endo*-*trig* cyclization. Nevertheless, the possibility of 5-*exo*-*trig* cyclizations has to be taken into account. For the desired polytwistane (**85**) the polymerization would need to occur exclusively *via* 6-*endo*-*trig* cyclizations (Scheme 87). Other possibilities are polymerizations with only 5-*exo*-*trig* cyclizations or with countless combinations of both regioselectivities, some of which are exercised in Scheme 87. The resulting hypothetical products exhibit interesting helical and circular scaffolds. A valuable conclusion of this thought experiment is that an eventual polymer formed by successive 5-*exo*-*trig* cyclizations converges on itself thereby presenting a dead-end in a polymerization. Assuming thermodynamic conditions, this may aid the formation of the desired polytwistane (**85**).

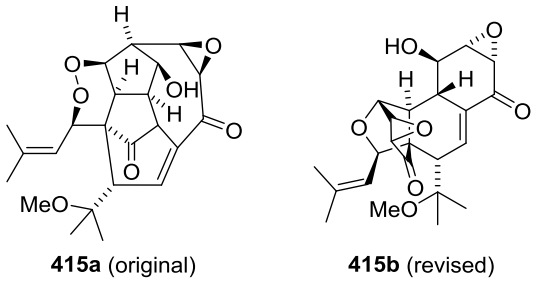


Scheme 87. Possible pathways of an initiator-biased acetylene polymerization. MM2 optimized structures of possible polymerization outcomes.

Despite the issue of regioselectivity, the initiator biased acetylene polymerization was identified as the most promising and feasible of the presented strategies. Advantages of this method are for instance the opportunity to modify the initiator compound to increase the helical bias. Additionally, the availability of transition metal catalysis as well as radical conditions for the polymerization process opens up a variety of options to adjust the outcome of the polymerization reaction.

Still, the initiator biased acetylene polymerization was not expected to result in the single formation of the desired product species. Therefore, to allow the identification of polytwistane (**85**) in complex reaction mixtures it was decided to calculate its ^{1}H NMR and ^{13}C NMR chemical shifts.

In recent times, the calculation of NMR spectra has evolved from being regarded as a specialist's tool to being widely applied by organic chemists.[170] This was made possible not only by advance in technology and computational chemistry but also by the availability of excellent protocols for experimentalists, often having no deeper understanding of the underlying computational methods.[171] The main use of the computational prediction of NMR spectra is the elucidation of chemical structures and the assignment of spectral data.[172] This resulted in several revisions of published natural product structures,[173] like in the classic case of hexacyclinol (**415**).[174]



415a (original) **415b** (revised)

Figure 14. Structural reassignment of the natural product hexacyclinol made possible by calculation of its NMR chemical shifts.[174]

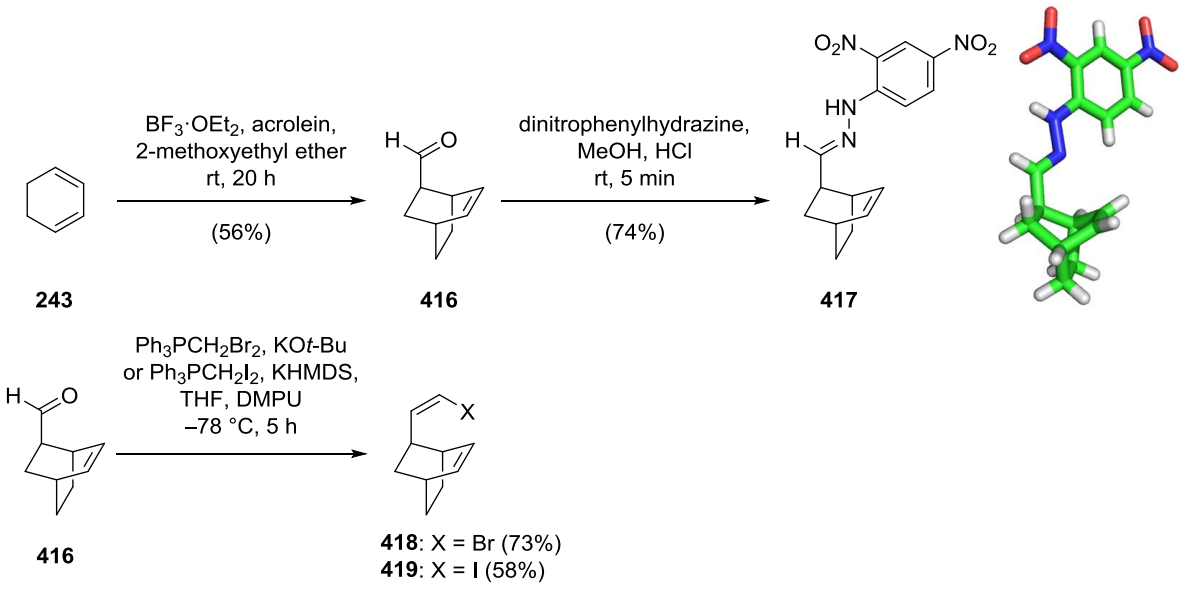
Beyond, the method was also used to establish reaction pathways,[175] analyze conformations[176] and characterize reactive intermediates. [177]

Since ideal polytwistane (**85**) should contain carbon and hydrogen atoms with an identical chemical environment, NMR spectroscopy is the method of choice for its identification. Therefore, the NMR chemical shifts of several oligotwistanes of different lengths (Figure 12) were to be calculated in order to determine the value of convergence, which is expected to correspond to the observed chemical shift of polytwistane (**85**).

3.2 Bicyclic Initiator Compounds

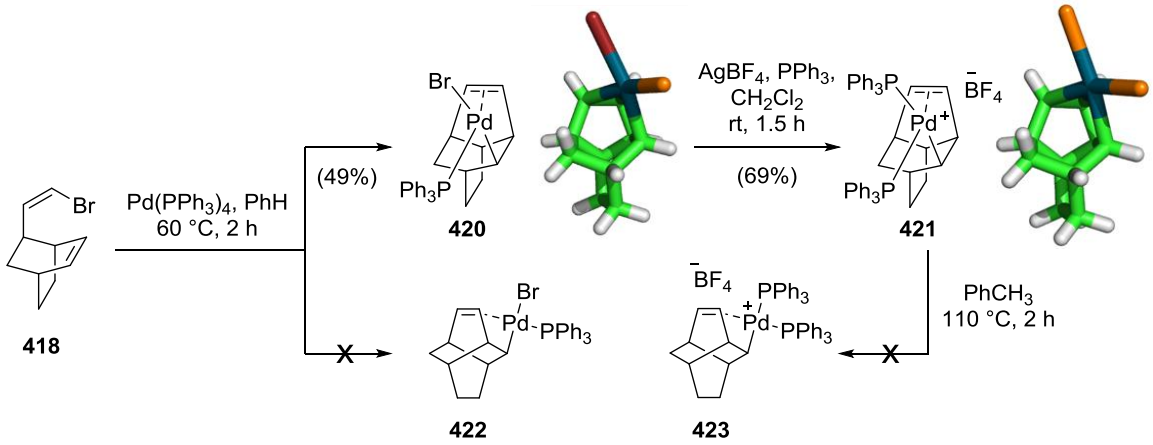
3.2.1 Synthesis and Cyclization Attempts of Haloalkenylbicyclo[2.2.2]octene

In order to investigate the feasibility of the envisioned acetylene polymerization, the crucial cyclization step was examined first. Therefore, bicyclic initiator molecules **418** and **419** were synthesized (Scheme 88). Known bicyclic aldehyde **416** was obtained from the Diels-Alder addition of acrolein to cyclohexadiene **243**.[178] The *endo* configuration of the aldehyde moiety was verified by conversion to its dinitrophenylhydrazone **417** and single crystal X-ray diffraction studies of this compound.[179] Conversion of bicyclic aldehyde **416** to (*Z*)-alkenyl bromide **418** and (*Z*)-alkenyl iodide **419** was accomplished using Stork-Zhao reactions.[180],[181] The alkenyl halide functionality was unequivocally established to be in the desired (*Z*)-configuration by the analysis of the vicinal coupling constant of the concerned olefinic protons. The observed value for this coupling constant was $^{3}J_{C9\text{-}H,C10\text{-}H}$ = 6.9 Hz (for **418**) and $^{3}J_{C9\text{-}H,C10\text{-}H}$ = 7.2 Hz (for **419**), as expected for *cis*-standing vicinal olefinic protons.[157]



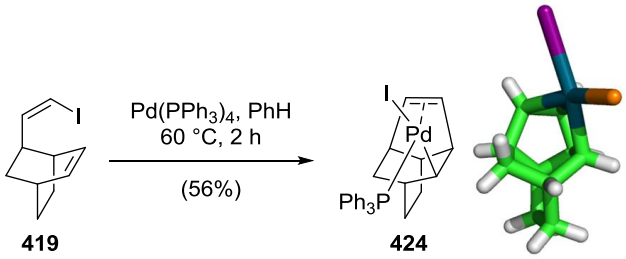
Scheme 88. Synthesis of bicyclic initiator compounds **418** and **419**.

With alkenyl halides **418** and **419** in hand, the stage was set to explore the crucial cyclization step of the proposed polymerization. In order to enable the unambiguous characterization of the cyclization product, it was decided to examine the cyclization first using a transition metal in stoichiometric quantity to bring about the reaction. Thus, alkenyl halide **418** was heated together with a stoichiometric amount of $Pd(PPh_3)_4$ in benzene (Scheme 89). However, only 5-*exo-trig* cyclization product, palladium complex **420**, instead of the desired 6-*endo-trig* cyclization product **422**, was isolated from the reaction mixture, as proven by single crystal X-ray diffraction. In an attempt to influence the selectivity of the reversible cyclization by adjusting the electronics of the system, neutral palladium complex **420** was converted to cationic palladium complex **421**. However, heating of species **421** in toluene did not lead to the formation of the desired twistene palladium complex **423**.



Scheme 89. Investigation of the crucial cyclization step on alkenyl bromide **418** using stoichiometric amounts of $Pd(PPh_3)_4$. Phenyl rings and BF_4^- are omitted from the X-ray structures for the sake of clarity. Color code: blue = Pd; green = C; orange = P; red = Br; white = H.

Submitting alkenyl iodide **419** to the same reaction conditions as before expectedly afforded only 5-*exo-trig* cyclization product **424**, as evidenced by single crystal X-ray diffraction (Scheme 90). Efforts to change the selectivity of the cyclization using lower temperatures, higher temperatures, longer reaction times or nickel as the transition metal on both substrates **418** and **419** either led to no conversion, the isolation of the 5-*exo-trig* cyclization products **420** and **424** or to decomposition.

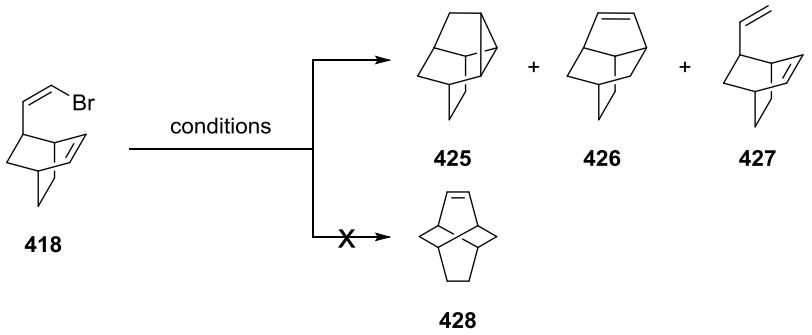


Scheme 90. Investigation of the crucial cyclization step on alkenyl iodide **419** with stoichiometric amounts of $Pd(PPh_3)_4$. Phenyl rings are omitted from the X-ray structure for the sake of clarity. Color code: blue = Pd; green = C; orange = P; purple = I; white = H.

Next, the cyclization was investigated using catalytic conditions with a hydride source to trap the intermediate palladium species. The simpler isolation and purification of the resulting hydrocarbon compounds, as compared to the previous metal complexes, allowed a more thorough screening of reaction conditions (Table 2). Initially the cyclization was conducted using Jeffery's conditions, at the same temperature as was used for the stoichiometric reactions, to afford 5-*exo-trig* cyclization product **426** and direct reduction product **427**, but not the desired twistene (**428**) (entry 1).[182] Running the reaction at lower temperatures resulted only in the re-isolation of starting material (entry 2) whereas higher temperatures afforded the same product mixture as before, albeit in lower yield (entry 3). This outcome might be rationalized by decomposition reactions at higher temperatures but could also be a consequence of the volatility of the products. Changing to a bidentate phosphine ligand (entry 4)

enabled the isolation of doubly cyclized cyclopropane **425**, beside isotwistene (**426**) and vinylbicyclo[2.2.2]octene **427** in improved yield, but also did not allow the observation of twistene (**428**). Subsequently, other variations of the reaction such as a chiral bidentate ligand (entry 5), a bulky ligand (entry 6), different solvent (entry 7) or the addition of a silver salt (entry 8) were tested but only led to isolation of the previously observed species. Using nickel instead of palladium was also unsuccessful resulting in decomposition (entry 9) or, in combination with MgH_2 as the hydride source, no conversion (entry 10). The identification of cyclopropane **425**, isotwistene (**426**) and vinylbicyclo[2.2.2]octene **427** was possible using analysis of NMR spectra and by comparison with published data.[183] Due to similar physical properties of the hydrocarbon compounds, purification presented problems. The best results were obtained using simple flash column chromatography with *n*-pentane as the mobile phase. However, it was not possible to achieve spectroscopic purity for every compound. The utilization of silica impregnated with silver nitrate as the stationary phase did not provide better results.[184] None of the tested conditions afforded the product of the desired 6-*endo*-*trig* cyclization, twistene (**428**).

Table 2. Investigation of the cyclization step on alkenyl bromide **418** using catalytic transition metal conditions.[a]

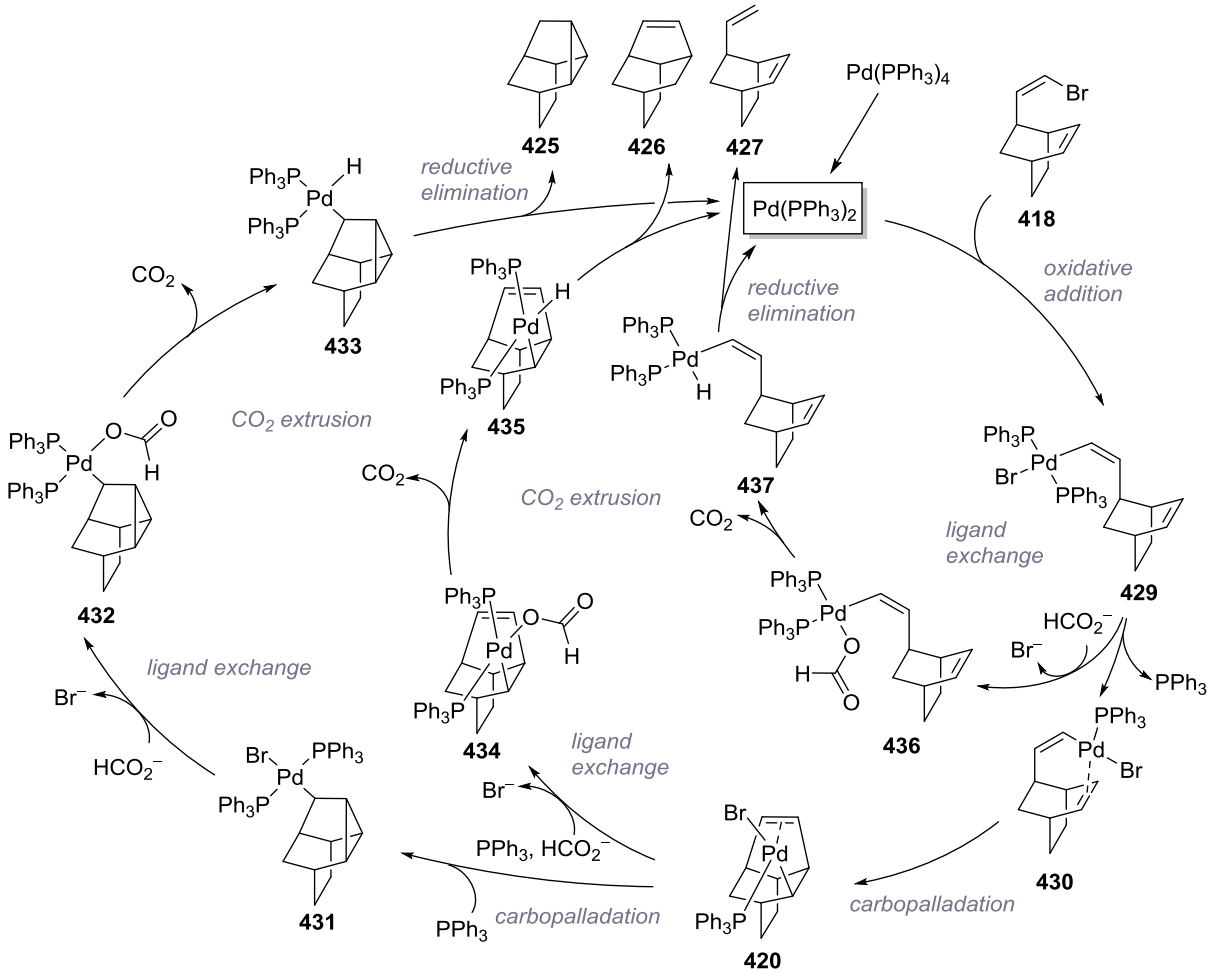


Entry	Transition metal	Additive	T [°C]	Yield [%][b]	Ratio 425 : 426 : 427[c]
1	$Pd(OAc)_2$	*n*-Bu_4NCl	60	58	0 : 1 : 1.2
2	$Pd(OAc)_2$	*n*-Bu_4NCl	rt	-[d]	-
3	$Pd(OAc)_2$	*n*-Bu_4NCl	160	35	0 : 1 : 1.3
4	$Pd(OAc)_2$	dppp	60	85	1 : 5.6 : 10.4
5	$Pd(OAc)_2$	*R*-BINAP	60	47	0 : 1 : 1.2
6	$Pd(OAc)_2$	CyJohnPhos	60	56	0 : 1 : 1.3
7[e]	$Pd(PPh_3)_4$	-	115	50	1.3 : 1 : 1.9
8	$Pd(PPh_3)_4$	$AgBF_4$	60	54	0 : 1 : 1.2
9	$Ni(PPh_3)_4$	-	60	-[f]	-
10[g]	$Ni(PPh_3)_4$	-	60	-[d]	-

(a) All reactions were carried out in degassed DMF employing $KHCO_2$ as the hydride source for 24 h unless stated otherwise. (b) Yield after flash column chromatography. (c) Ratio based on isolated yield. Due to the volatility of the products, the reported ratio might not represent the actual outcome of the reaction. (d) Starting material was re-isolated. (e) The reaction was performed in degassed $PhCH_3$. (f) Decomposition of starting material was observed. (g) The reaction was carried out employing MgH_2 as the hydride source.

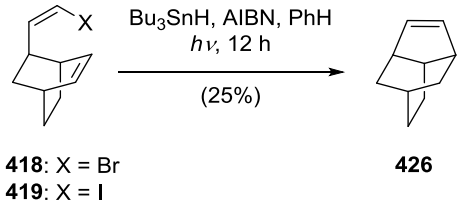
The formation of the three observed hydrocarbon skeletons **425**, **426** and **427** is assumed to proceed according to the mechanism shown in Scheme 91. The catalytic cycle begins with the oxidative addition of the reactive palladium species to alkenyl bromide **418** resulting in alkenyl palladium complex **429**. Intramolecular coordination of the second double bond then leads to the displacement of a phosphine ligand affording complex **430** which undergoes carbopalladation by a 5-*exo*-*trig* cyclization resulting in alkyl palladium complex **420**. This complex was isolable under stoichiometric conditions (Scheme 89). Another carbopalladative 3-*exo*-*trig* cyclization then gives cyclopropane **431**. This cyclization can also be regarded as a homoallyl/cyclopropylcarbinyl rearrangement. A subsequent ligand exchange resulting in formate complex **432** followed by *β*-hydride elimination with concomitant CO_2 extrusion yields palladium hydride **433** which after reductive elimination affords cyclopropane **425**.

If the ligand exchange occurs on palladium complex **420**, the result is palladium formate **434**, which after *β*-hydride elimination and subsequent reductive elimination affords mono-cyclized product **426**. Analogously, the formation of diene **427** is the product of ligand exchange on palladium alkenyl complex **429** and ensuing *β*-hydride elimination of formate complex **436** which is followed by reductive elimination of palladium from hydride complex **437**, giving rise to hydrocarbon **427**.



Scheme 91. Catalytic cycle for the reaction of alkenyl bromide **418** with $Pd(PPh_3)_4$.

As the transition metal-catalyzed approach did not seem viable to obtain the desired result, reductive radical cyclization conditions were investigated for the crucial cyclization step. Thus, a solution of alkenyl bromide **418** or alkenyl iodide **419** in benzene was irradiated in the presence of AIBN and tributyltin hydride with a 260 W sunlamp (Scheme 92). Monitoring of the reaction by NMR showed partial conversion to 5-*exo*-*trig* cyclization product **426**. Full conversion was not achieved under these conditions, even upon prolonged reaction times. Also, no formation of another unsaturated species such as twistene (**428**) was observed. As the formation of isotwistene (**426**) was previously reported by the group of Gravel using similar conditions and the 5-*exo*-*trig* cyclization is established to be the favored process under radical conditions, it was decided to investigate other options to achieve the desired 6-*endo*-*trig* cyclization.[185]



Scheme 92. Radical reductive cyclization of simple initiator compounds **418** and **419**. Yield based on ^{1}H NMR spectroscopy.

3.2.2 Synthesis and Cyclization Attempts of Methylated Haloalkenylbicyclo[2.2.2]octene

The introduction of methyl substituents on the bicyclic scaffold of the initiator compounds was identified as a possible way to influence the steric and electronic parameters and thus possibly also the regioselectivity of the cyclization reaction. In order to increase the steric encumbrance of the transition metal in the undesired 5-*exo*-*trig* cyclization mode, C2 was chosen as one site for the installation of a methyl group (Figure 15). To induce a subtle change of the position of the alkenyl halide handle in respect to the other alkene moiety, C5 was selected as a second methyl substitution site. As a result, the two monomethyl derivatives **438** and **439**, as well as dimethylderivative **440** were planned to be prepared.

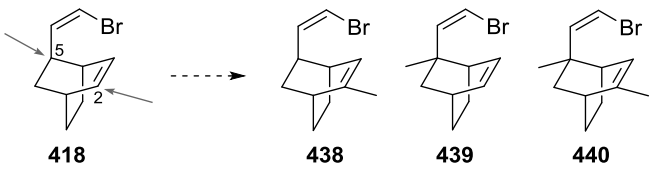
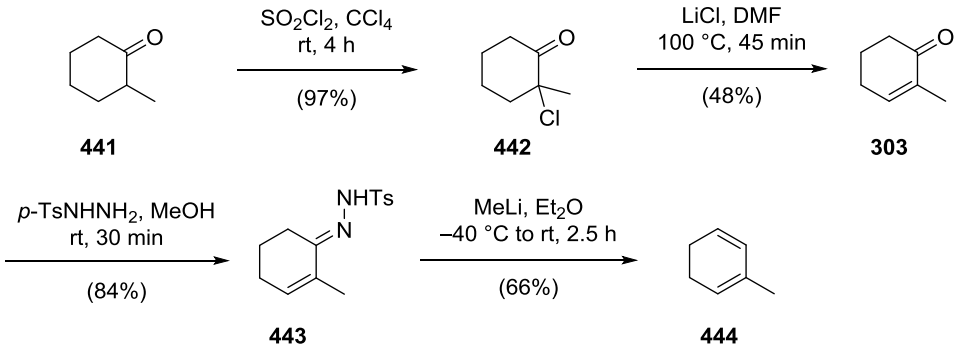


Figure 15. Planned modification of the initiator compounds to influence the steric and electronic parameters of the cyclization reaction.

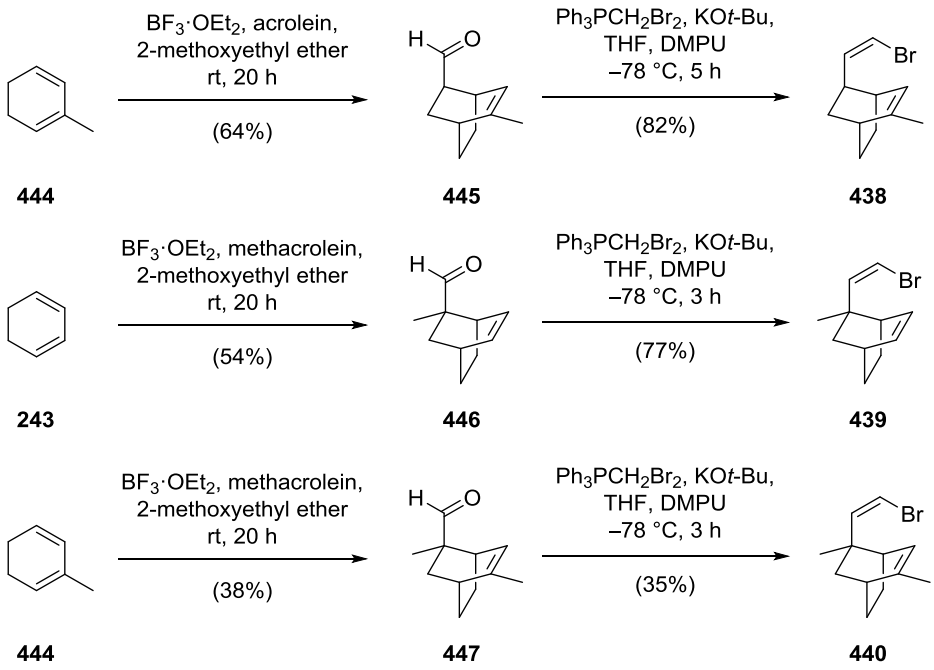
In order to synthesize the modified initiator compounds **438**, **439** and **440**, methylcyclohexadiene **444** was required. It was obtained in a sequence of four known steps from commercially available 2-methylcyclohexanone (**441**) (Scheme 93).[186] Thus, chlorination of the starting material using

sulfuryl chloride afforded chlorocyclohexanone **442**, which after elimination of HCl resulted in cyclohexenone **303**. Subsequent Shapiro olefination *via* tosylhydrazone **443** then gave rise to methylcyclohexadiene **444**.



Scheme 93. Synthesis of methylcyclohexadiene **444**.

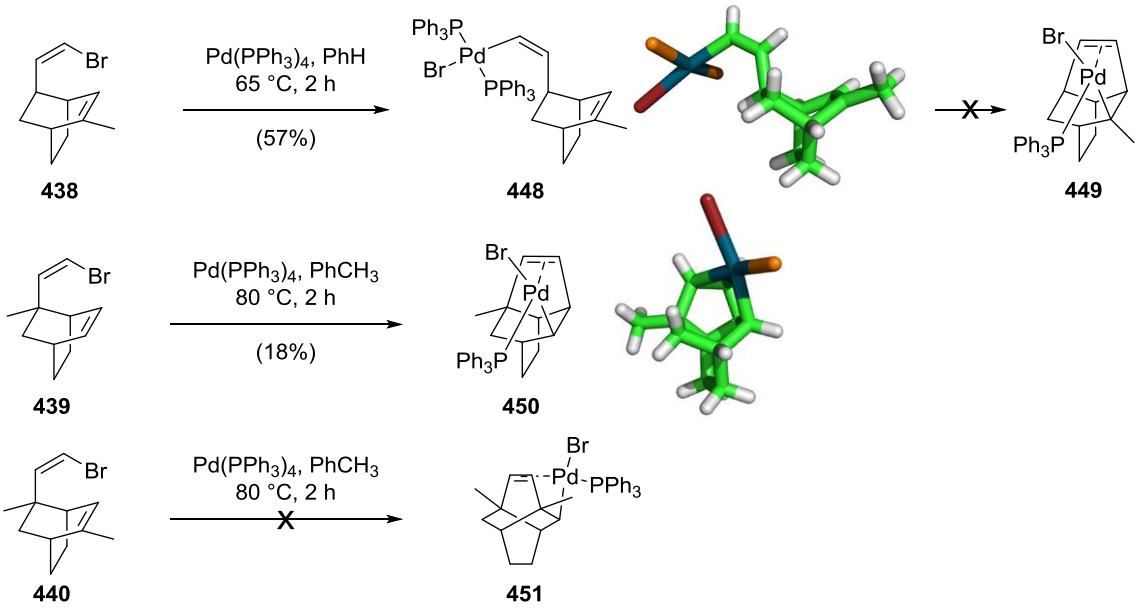
The synthesis of the methylated initiator compounds was carried out analogously to the preparation of compound **418** (Scheme 88). The Diels-Alder addition of acrolein to methylcyclohexadiene **444** afforded methylcarbaldehyde **445** (Scheme 94). The combination of cyclohexadiene **243** with methacrolein resulted in isomeric methylcarbaldehyde **446**. For the dimethylsubstituted analog **447**, methylcyclohexadiene **444** was added to methacrolein in the Diels-Alder reaction. Subsequent Stork-Zhao reactions allowed for the synthesis of the respective bromoalkenyl compounds **438**, **439** and **440**.



Scheme 94. Synthesis of methyl substituted bicyclic initiator compounds **438**, **439** and **440**.

Submitting alkenyl bromide **438** to stoichiometric palladation conditions led to the isolation of alkenyl palladium complex **448** (Scheme 95). This compound is one of only a few alkenyl palladium

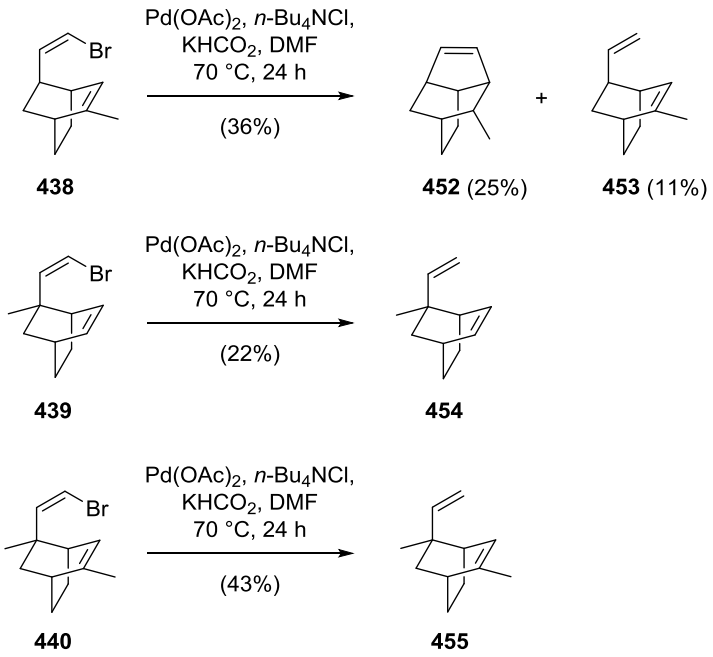
complexes characterized with single crystal X-ray diffraction.[187] The observation of oxidative addition product **448** can be rationalized by the highly sterically encumbered intermediate **449** which would result from a potential 5-*exo-trig* cyclization. As a consequence, the 6-*endo-trig* cyclization appears to posess a high activation barrier, as only uncyclized species **448** was observed. On the contrary, the reaction of isomeric alkenyl bromide **439** with a stoichiometric amount of $Pd(PPh_3)_4$ afforded 5-*exo-trig* cyclized complex **450**, similarly characterized by single crystal X-ray diffraction. From the reaction of dimethyl derivative **440** using the same conditions no crystals were obtained. Upon prolonged reaction times decomposition was observed. In no case a product resulting from a 6-*endo-trig* cyclization, such as twistene complex **451**, was found.



Scheme 95. Investigation of the crucial cyclization step on methyl substituted bicyclic initiator compounds using stoichiometric amounts of $Pd(PPh_3)_4$. Phenyl rings are omitted from the X-ray structures for the sake of clarity. Color code: blue = Pd; green = C; orange = P; red = Br; white = H.

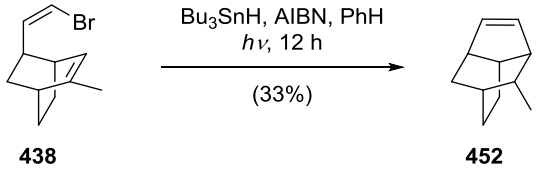
Attempts to cyclize alkenyl bromide **438** under catalytic conditions provided only undesired 5-*exo-trig* cyclization product **452**, along with the product of direct reduction **453** (Scheme 96). Taken together with the above mentioned isolation of alkenyl palladium complex **448**, the observation of isotwistene **452** indicates that a corresponding 5-*exo-trig* palladium intermediate, such as **449**, forms during the reaction but presumably has a very short lifetime. This species is either trapped immediately by a formate to result in isotwistene **452** or fragments in a *β*-carbon elimination to intermediate **448**, leading to direct reduction product **453**.

In the case of isomeric alkenyl bromide **439** transition metal catalytic conditions only yielded diene **454**, as the product of direct reduction. Analysis of the crude reaction mixture also showed other species, which might correspond for example to the product of 5-*exo-trig* cyclization, but a clean spectroscopic characterization was not possible due to co-polarity of other impurities. For alkenyl bromide **440** these conditions only afforded diene **455**.



Scheme 96. Investigation of the cyclization step on methyl substituted bicyclic initiator compounds using catalytic transition metal conditions.

Alkenyl bromide **438** was also submitted to reductive radical conditions to effect the cyclization (Scheme 97). NMR spectroscopy established only partial conversion to methylisotwistene **452**, even after long reaction times. It was not possible to identify any twistene structure from the reaction mixture.

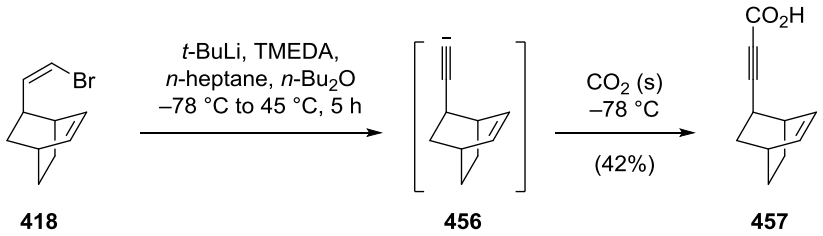


Scheme 97. Radical reductive cyclization of methyl substituted initiator compound **438**. Yield based on ^{1}H NMR spectroscopy.

3.2.3 Other Cyclization Attempts

As all previous attempts to achieve the 6-*endo*-*trig* cyclization using transition metal catalysis or reductive radical conditions proved futile, other possibilities were explored. Initiator compounds **418** and **419** were used for this purpose as they were easily available on scale due to their short two-step syntheses (Scheme 88). First, the cyclization was investigated using a carbometalation reaction with a main group metal.[188] Apart from the possibility to trigger a different regioselectivity, this method gives the advantage to trap the intermediately generated anion with any desired electrophile. Thereby the isolation and separation of the reaction products is greatly simplified as compared to the previous metal complexes or hydrocarbon compounds. Therefore, alkenyl bromide **418** was subjected to

carbolithiation conditions (Scheme 98). However, even using a solvent system that allows the reaction to be run at temperatures higher than room temperature, no cyclized products were formed. Only propiolic acid derivative **457**, as a result of dehydrohalogenation *via* acetylide **456**, was observed.



Scheme 98. Cyclization attempt using carbolithiation conditions.

Subsequently, several atom transfer cyclization conditions were screened in order to change the selectivity of the cyclization (Table 3). Thereby, the occurrence of halide atoms in the products would be advantageous for their isolation, due to the reduced volatility compared to the parent hydrocarbon compounds. First attempts on alkenyl bromide **418** used Cu^{I}-based atom transfer radical cyclization conditions at different temperatures (entries 1, 2) but did not provide any conversion.[189] The same result was found for the use of Cu^{I}-salts in combination with common ligands in different solvents (entries 3, 4) or if alkenyl iodide **419** was used as the substrate (entries 5, 6). The use of Bu_6Sn_2 or AIBN as the radical initiator in combination with irradiation by a sunlamp led to partial isomerization of the (*Z*)-alkenyl halide moiety (entries 7, 8).[190],[191] Interestingly, even after long irradiation times the observed ratio of (*Z*)- to (*E*)-isomer did not exceed 3 : 1, with the presumably less stable (*Z*)-isomer as the major isomer. The isomerization was evidenced by a marked increase of the vicinal coupling constant of the protons at the alkenyl iodide moiety from $^{3}J_{C9\text{-}H,C10\text{-}H} = 7.2$ Hz to $^{3}J_{C9\text{-}H,C10\text{-}H} = 14.4$ Hz (Figure 16), as expected according to reported data.[157]

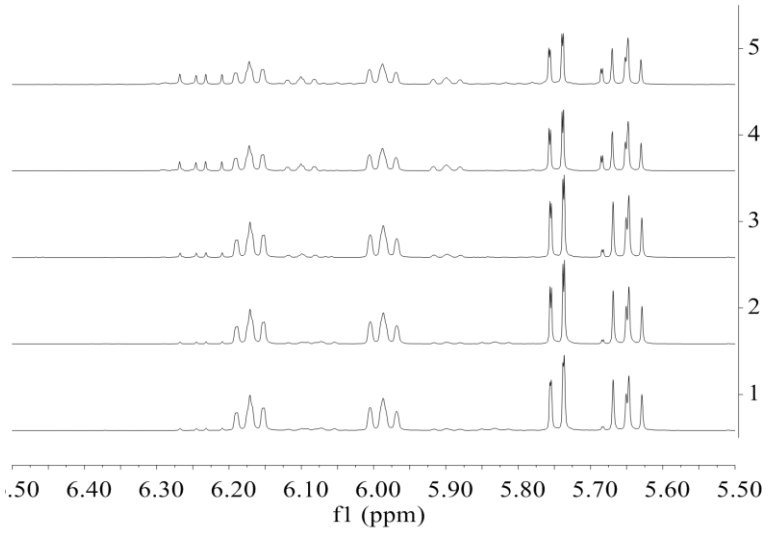
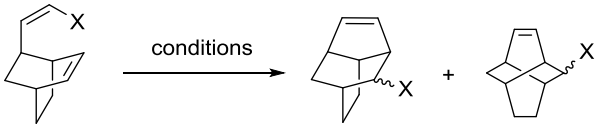


Figure 16. Comparison of the relevant range from ^{1}H NMR spectra of the attempted atom transfer cyclization: starting material (1), after addition of AIBN (2), after 2.5 h (3), 19 h (4) and 43 h (5) of irradiation.

Exhaustive characterization of the observed (*E*)-alkenyl iodide was not possible due to purification problems resulting from the co-polarity with (*Z*)-alkenyl iodide **419**. No indication for a cyclization was found, in form of a species with reduced number of olefinic signals in ^{1}H NMR. Employing another solvent (entries 9, 10) resulted in no conversion of starting material. The same result was found using a more intense Hg-lamp (entry 11) and in the combination of this light source with Bu_6Sn_2 or AIBN (entries 12, 13). Similarly, no reaction was observed under these conditions if alkenyl bromide **418** was used as the starting material (entry 14).

Table 3. Screening of atom transfer cyclization conditions for the facilitation of the desired 6-*endo*-*trig* mode.[a]



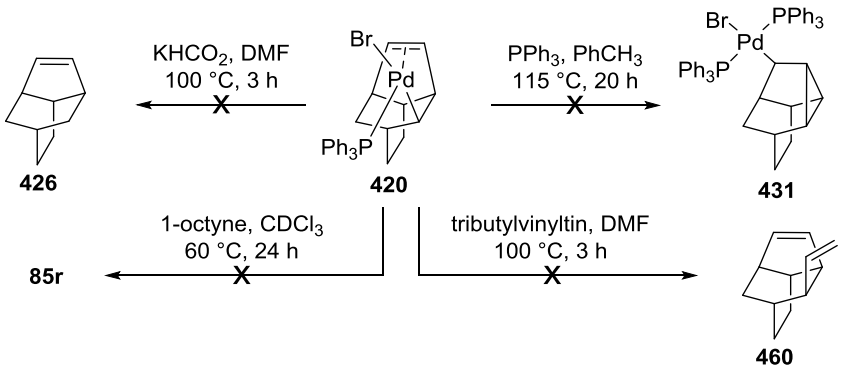
418: X = Br
419: X = I

458 **459**

Entry	X	Reagents	Solvent	Irradiation	T [°C]	t [h]	Result
1[b]	Br	CuBr	MeCN	-	110	16	no conversion
2[b]	Br	CuBr	MeCN	-	130	72	no conversion
3[b]	Br	CuBr, TPMA, AIBN	$PhCH_3$	-	80	16	no conversion
4[b]	Br	CuBr, bipy	DCE	-	80	16	no conversion
5[b]	I	CuI	MeCN	-	80	72	no conversion
6[b]	I	CuI, bipy	DCE	-	80	72	no conversion
7[c]	I	Bu_6Sn_2	C_6D_6	275 W	50[d]	67	(*Z*)- to (*E*)- isom.[e,f]
8[c]	I	AIBN	C_6D_6	275 W	50[d]	67	(*Z*)- to (*E*)- isom.[e,f]
9[c]	I	Bu_6Sn_2	CD_3CN	275 W	50[d]	67	no conversion[e]
10[c]	I	AIBN	CD_3CN	275 W	50[d]	67	no conversion[e]
11[c]	I	-	C_6D_6	450 W	rt	5	no conversion[e]
12[c]	I	AIBN	C_6D_6	450 W	rt	5	no conversion[e]
13[c]	I	Bu_6Sn_2	C_6D_6	450 W	rt	5	no conversion[e]
14[c]	Br	AIBN	C_6D_6	450 W	rt	5	no conversion

(a) All reactions were monitored by ^{1}H NMR spectroscopy. (b) Reaction was run in a sealed tube. (c) Reaction was performed in an NMR tube. (d) The temperature was a result of the position of the NMR tube distanced by 5 cm from the hot light source. (e) The reaction mixture changed color during the irradiation from colorless to purple. (f) According to analysis of the ^{1}H NMR spectra a 3 : 1 ratio of (*Z*)- to (*E*)-isomer was observed at the maximum.

Finally, the isolated palladium complex **420** was utilized for functionalization and polymerization attemps (Scheme 99). However, all efforts to perform hydride coupling to isotwistene **426**, cyclization to cyclopropyl palladium complex **431**, Stille coupling to vinylisotwistene **460** or polymerization reactions using acetylene derivatives were met with failure. This reactivity was also not changed by the addition of $AgBF_4$ to remove the bromide and thus activate the complex.



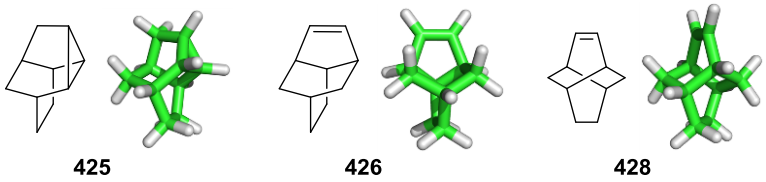
Scheme 99. Futile efforts to use palladium complex **420** as starting material for functionalizations or polymerization.

Due to the continued failure of various methods to deliver the desired 6-*endo-trig* cyclization products, the experimental approach using bicyclic initiators, such as **418**, **419**, **438**, **439** and **440**, was abandoned.

3.2.4 Thermodynamic Considerations

In order to rationalize the reluctance of the bicyclic initiator compounds to undergo the cyclization in the desired 6-*endo-trig* mode, it was decided to utilize computational methods. All geometry optimization and frequency calculations were carried out with Gaussian03[192] using the B3LYP[193] density functional in combination with the following basis sets: The 6-31G(d) and 6-311+G(2d,p)[194] basis sets were employed for all elements except palladium, for which the SDD and LANL2DZ[195] basis sets were used. Due to the rigidity of the examined systems no conformational analysis was performed, as the geometry optimization could be reasonably assumed to provide the global minimum. To get an impression of the thermodynamics involved in the reactions, the observed cyclization products were compared with the respective desired 6-*endo-trig* cyclization products. Indeed, in agreement with the experimental observations, the calculation of the hydrocarbon compounds resulting from a potential reductive cyclization showed that observed isotwistene **426** is the thermodynamically most stable of the three isomers (Table 4, entries 1, 2). By comparison, desired twistene (**428**) is more than 7 kcal·mol^{-1} less stable than **426**, as shown by both computational methods employed (entries 1, 2). The experimentally also observed cyclopropane **425** is 1.9 kcal·mol^{-1} (entry 1) or 3.9 kcal·mol^{-1} (entry 2) less stable than isotwistene **426** depending on the employed basis set. For the calculation of the products from stoichiometric palladation reactions, a modified X-ray structure of complex **420**, with the phosphine ligand being simplified to PMe_3, was used. The results of the calculations (Table 5, entries 1, 2, 3) were less clear than for the hydrocarbon compounds, indicating similar energies for 5-*exo-trig* cyclization product **461** and 6-*endo-trig*-cyclization product **462**.

Table 4. Computational results for the possible hydrocarbon products resulting from transition metal-catalyzed cyclization or reductive radical cyclization (B3LYP/basis set).[a]

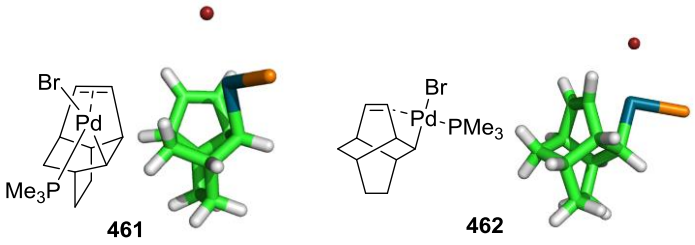


425 426 428

Entry	Basis Set	Relative Energy 425	Relative Energy 426	Relative Energy 428
1	6-31G(d)	1.9	0	7.1
2	6-311+G(2d,p)	3.9	0	7.3

(a) Relative energies are given in kcal·mol^{-1}. Models are shown using coordinates from B3LYP/6-31G(d) level.

Table 5. Computational results for the possible palladium complexes resulting from stoichiometric transition metal cyclization (B3LYP/basis set).[a]

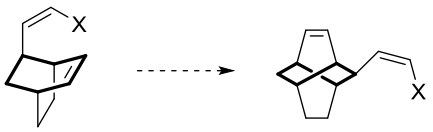


461 462

Entry	Basis Set	Relative Energy 461	Relative Energy 462
1	6-31G(d)/SDD	0	0.6
2	6-311+G(2d,p)/SDD	0	0.7
3	6-311+G(2d,p)/LANL2DZ	0	1.0

(a) Relative energies are given in kcal·mol^{-1}. Models are shown using coordinates from B3LYP/6-311+G(2d,p)/LANL2DZ level. Methyl groups are omitted for the sake of clarity.

Experimental as well as theoretical results indicate that the cyclohexane moiety in the boat conformation, as contained in the bicyclic precursors **418** and **419**, is not enough to bias the system toward the desired cyclization mode (Scheme 100). A reasonable modification to increase the helical propensity toward the 6-*endo-trig* cyclization might be the incorporation of the twist-boat motive in the precursor scaffold. Thus, the expanded precursors, alkenyl bromide **463** and alkenyl iodide **464**, which contain the skeleton of twistene (**428**), were investigated next.



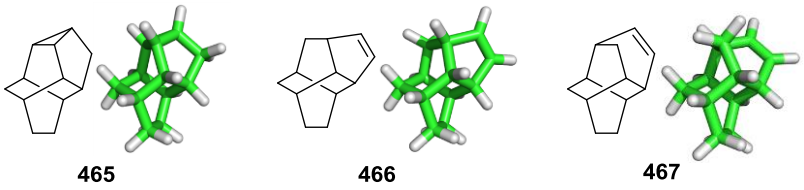
418: X = Br
419: X = I

463: X = Br
464: X = I

Scheme 100. Expansion of the precursor scaffold to increase the bias toward the desired helicity.

To test this hypothesis, a computational analysis of the possible cyclization products resulting from expanded precursors **463** and **464** was performed. The results from the calculation of the hydrocarbon compounds showed that with this modification the product of 6-*endo-trig* cyclization **467** is stabilized by ~2.5 kcal·mol^{-1} in respect to the product of the undesired 5-*exo-trig* cyclization **466** (Table 6, entries 1, 2). However, doubly cyclized cyclopropane **465** is either the most stable of the three isomers (entry 1) or very close in energy to ditwistene (**467**) (entry 2). In case of the palladium complexes **468** and **469**, all calculations showed that the desired 6-*endo-trig* cyclized isomer **469** is stabilized by more than 3 kcal·mol^{-1} in respect to 5-*exo-trig* cyclization product **468** (Table 7, entries 1, 2, 3). These results indicate that the desired 6-*endo-trig* might indeed be facilitated by this modification.

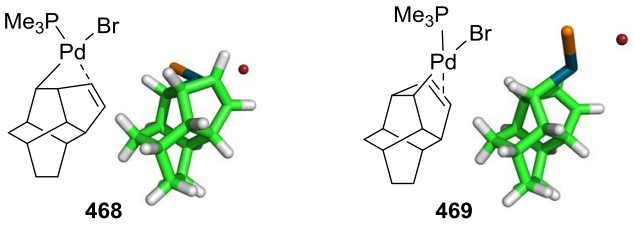
Table 6. Computational results for the possible hydrocarbon products resulting from transition metal-catalyzed cyclization or reductive radical cyclization (B3LYP/basis set).[a]



Entry	Basis Set	Relative Energy 465	Relative Energy 466	Relative Energy 467
1	6-31G(d)	−1.8	2.7	0
2	6-311+G(2d,p)	0.1	2.5	0

(a) Relative energies are given in kcal·mol^{-1}. Models are shown using coordinates from B3LYP/6-31G(d) level.

Table 7. Computational results for the possible palladium complexes resulting from stoichiometric transition metal cyclization (B3LYP/basis set).[a]



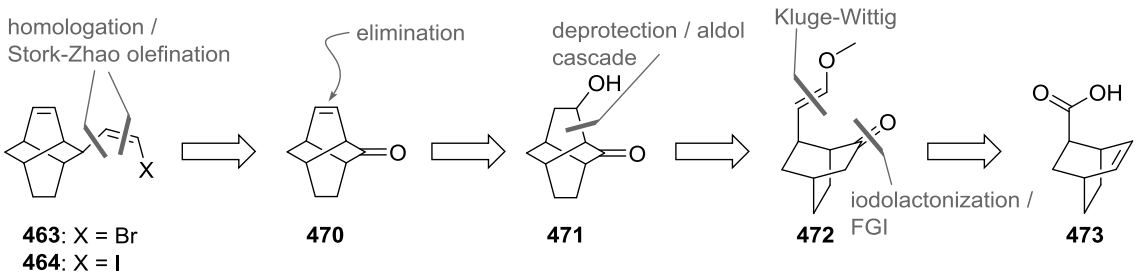
Entry	Basis Set	Relative Energy 468	Relative Energy 469
1	6-31G(d)/SDD	3.3	0
2	6-311+G(2d,p)/SDD	3.3	0
3	6-311+G(2d,p)/LANL2DZ	3.1	0

(a) Relative energies are given in kcal·mol^{-1}. Models are shown using coordinates from B3LYP/6-311+G(2d,p)/LANL2DZ level. Methyl groups are omitted for the sake of clarity.

3.3 Tricyclic Initiator Compounds

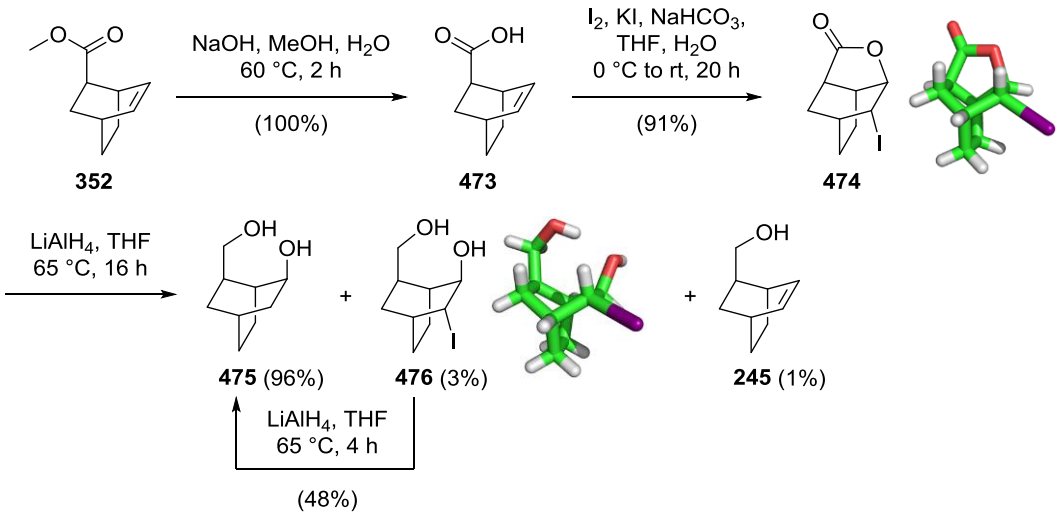
3.3.1 Synthesis of Tricyclic Precursors *via* Deprotection – Cyclization Cascade

Motivated by the thermodynamic predictions, the next objective was to synthesize the initiator compounds **463** and **464**, which incorporate the twistene skeleton. In the initial retrosynthetic analysis these compounds were traced back to twistenone **470** *via* homologation and Stork-Zhao olefination reactions (Scheme 101). This was again planned to be accessed in an elimination reaction from ketoalcohol **471**. The latter compound could arise from a deprotection / intramolecular aldol cascade of enol ether **472**, which should be readily available from known carboxylic acid **473** by iodolactonization, functional group interconversion and homologation reactions.[196]



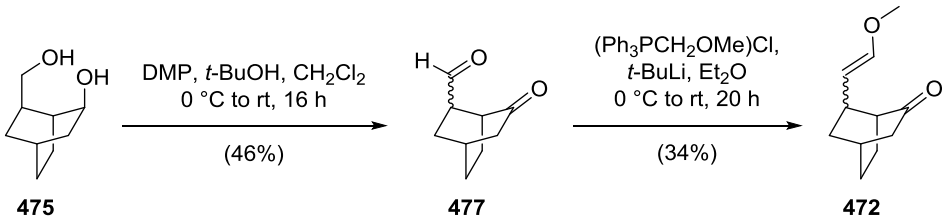
Scheme 101. Initial retrosynthetic analysis of alkenyl halides **463** and **464**.

Thus, bicyclo[2.2.2]octeneester **352**, which was available from the synthesis of tritwistane (**288**), was saponified to carboxylic acid **473** (Scheme 102).[196] A subsequent iodolactonization provided iodolactone **474**. Reduction of this species with $LiAlH_4$ in refluxing THF afforded desired diol **475** along with alkenol **245** and iodohydrine **476**.[197] The latter compound presumably is formed as an intermediate during the reduction to diol **475** and can be transformed to the same by re-subjection to the reduction conditions.



Scheme 102. Synthesis of diol **475** from bicyclo[2.2.2]octeneester **352**.

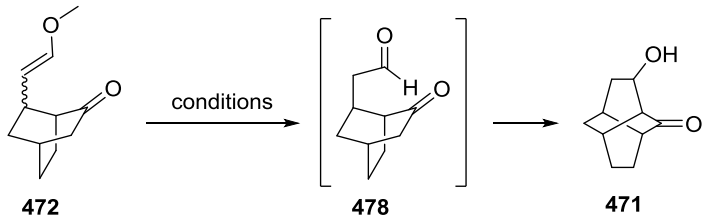
Unfortunately, the oxidation of diol **475** provided formylbicyclooctane **477** only in moderate yields and in an unseparable 1 : 1 mixture of isomers regarding the position of the formyl group (Scheme 103). Of several tested oxidation conditions, including PCC, Ley oxidation and Swern oxidation, the best yield was achieved using DMP but all methods gave the same mixture of diastereomers. As the planned aldol cyclization would differentiate between both diastereomers, the mixture was carried on to the next step. Homologation using the Kluge-Wittig procedure afforded the desired enol ether **472** in enough quantity to investigate the deprotection / intramolecular aldol cascade.[198]



Scheme 103. Synthesis enol ether **472** as the precursor for the planned deprotection/aldol cascade.

In order to enable the envisioned cascade, standard conditions for the deprotection of the enol ether moiety were tested.[198] This approach should at least allow the isolation of intermediate 1,5-dicarbonyl **478** (Table 8). The first attempt, using *p*-TsOH at ambient temperature (entry 1) indicated the liberation of the aldehyde moiety but did not allow the isolation of a distinct product species. Further efforts at higher temperatures (entry 2) or employing other acid sources (entries 3, 4) only led to decomposition of starting material. In no case was it possible to isolate the desired hydroxytwistanone **471** or the product of deprotection **478**.

Table 8. Attempted deprotection / intramolecular aldol cyclization to generate the twistane scaffold.[a]

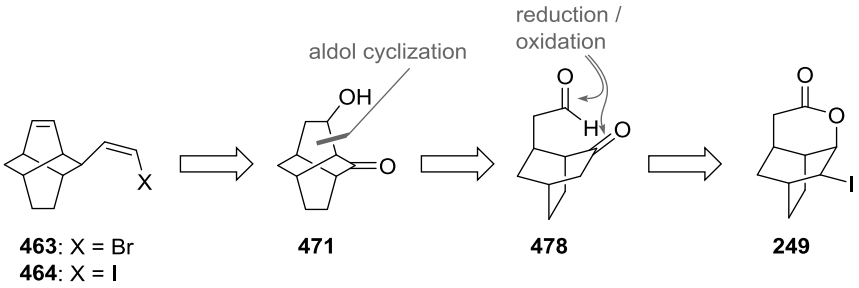


Entry	Reagent	Solvent	T [°C]	Result
1	*p*-TsOH	PhH	rt	traces of **478**[b]
2	*p*-TsOH	PhH	50 °C	decomposition[c]
3	$HClO_4$	dioxane	rt	decomposition[c]
4	HCl	acetone	50 °C	decomposition[c]

(a) All reactions were run until the starting material was completely consumed, according to TLC. (b) According to mass spectrometry. (c) Formation of a multitude of products none of which could be characterized cleanly.

3.3.2 Synthesis of Tricyclic Precursors *via* Stepwise Homologation - Cyclization

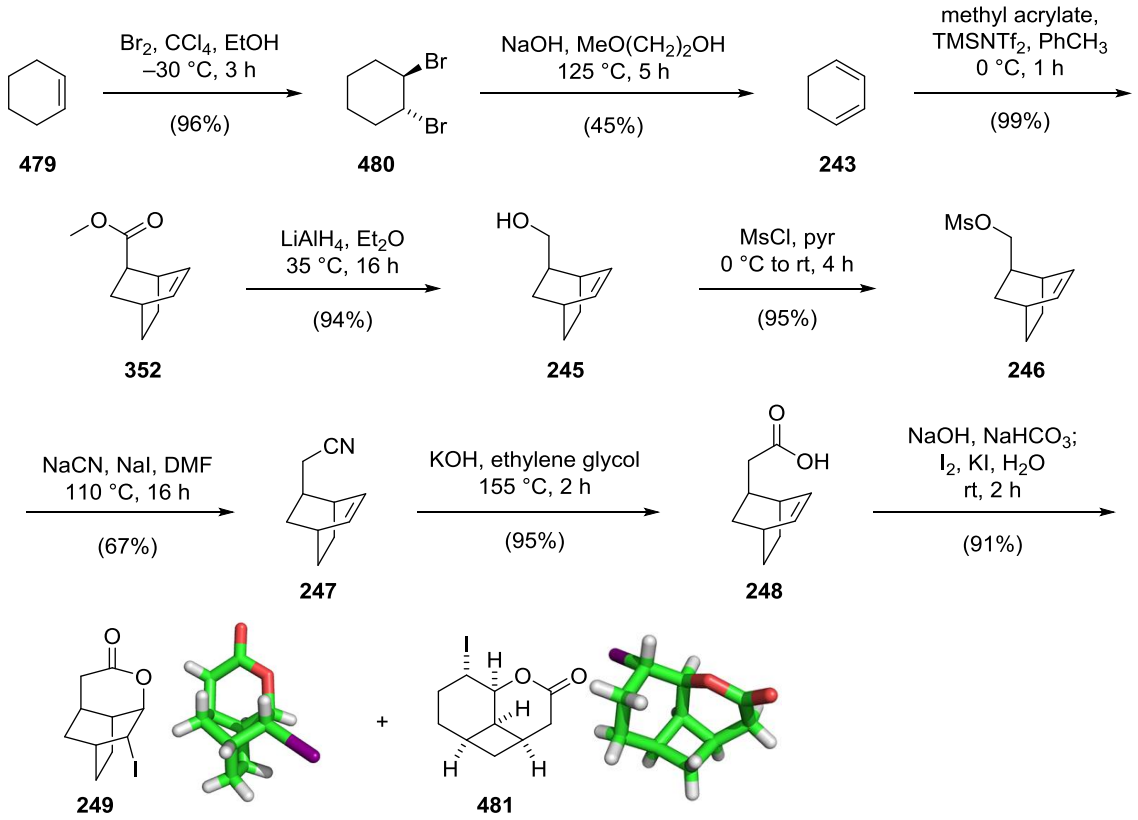
In parallel, a second retrosynthetic analysis was pursued, which utilized the same strategy to generate the twistane skeleton *via* an aldol cyclization but building on another homologation sequence (Scheme 104). Hence, alkenyl halides **463** and **464** should originate as before from keto alcohol **471** (Scheme 101). This was traced back *via* an aldol cyclization to dicarbonyl **478**, which should be obtained in subsequent functional group interconversions from known iodolactone **249**.[118] The latter compound constitutes a homolog to formerly synthesized iodolactone **474**.



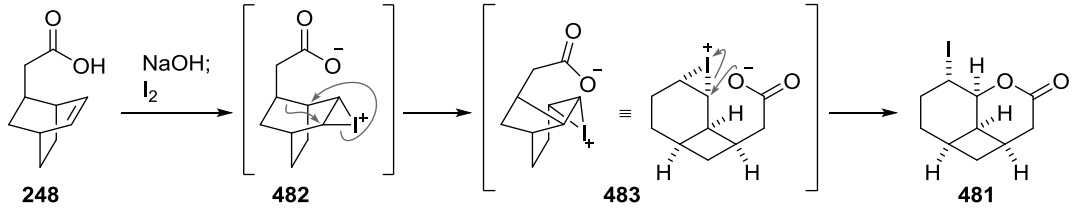
Scheme 104. Second retrosynthetic analysis of alkenyl halides **463** and **464** *via* aldol cyclization of keto alcohol **478**.

In order to access alkenyl halides **463** and **464** on scale for the planned screening of cyclization conditions, a large amount of expensive cyclohexadiene **243** was necessary. Consequently, cyclohexadiene **243** was synthesized cost effectively from cyclohexene (**479**) *via* bromination to dibromide **480** and subsequent double elimination, starting on a n = 3 mol scale (Scheme 105).[199] Transformation to bicycloester **352** was carried out as previously described during the synthesis of tritwistane (**288**) using $TMSNTf_2$ to catalyze the Diels-Alder addition of methyl acrylate to cyclohexadiene **243**. The next steps were performed analogously to Whitlock's synthesis of twistane (**254**).[118] Therefore, bicycloester **352** was reduced to alcohol **245**, which was then converted to mesylate **246**. Ensuing S_N2 displacement of the mesylate group by a cyanide led to nitrile **247** which was hydrolyzed under basic conditions to carboxylic acid **248**. From the iodolactonization reaction of carboxylic acid **248**, rearranged iodolactone **481** was isolated in minute amounts beside the desired iodolactone **249**. Both isomeric iodolactones were characterized unambiguously by single crystal X-ray diffraction. Over the whole 8 step sequence from cyclohexene (**479**) to iodolactone **249** an overall yield of 22% was achieved, allowing the multi-gram synthesis of iodolactone **249**. For the formation of isomeric iodolactone **481**, which incorporates a rare tricyclic lactone scaffold,[200] the following mechanism might be reasonable (Scheme 106). Intermediately formed iodonium ion **482** rearranges in a suprafacial [1,3] alkyl shift with inversion of the migrating group to cyclobutane containing iodonium ion **483**. This then gets trapped in a 6-*exo-tet* cyclization by the carboxylate moiety to result in iodolactone **481**. The isolation of this species, which was formed in a yield of approximately 0.4%, was only possible due to the large scale on which the iodolactonization reaction was run. This finding illustrates the intriguing and unanticipated chemistry that often takes place

during routine operations but remains undiscovered due to the impossibility to isolate the resulting species on the scales usually used in total synthesis.

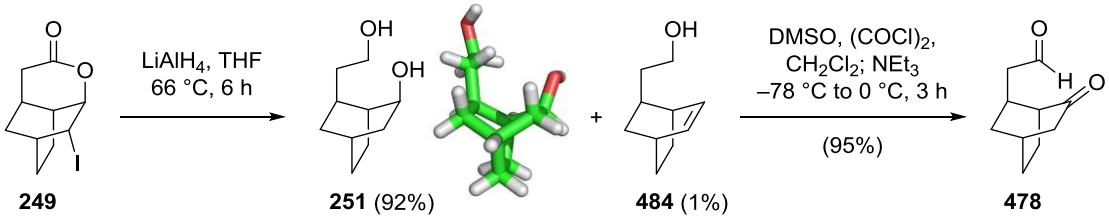


Scheme 105. Synthesis of iodolactone **249** according to Whitlock's synthesis of twistane (**254**).[118]



Scheme 106. Presumable mechanism for the formation of iodolactone **481**.

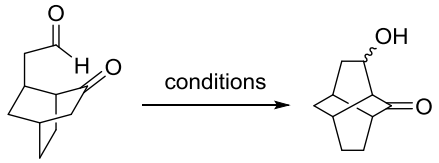
Next, iodolactone **249** was reduced in one step to diol **251**, also affording alkenol **484** as a minor side product (Scheme 107).[197] Subsequent Swern oxidation provided keto aldehyde **478** in excellent yield. Thus, the plan to isolate the precursor **478** of the planned aldol cyclization worked out.



Scheme 107. Synthesis of precursor **478** for the aldol cyclization.

With keto aldehyde **478** in hand, the stage was set for the formation of the twistane core. As the aldol cyclization of similar 1,5-dicarbonyls was investigated thoroughly by various groups, the most prevalent conditions to effect this transformation were identified from the literature.[201] In the first attempt, keto aldehyde **478** was heated with HCl in acetone to provide a mixture of the desired hydroxytwistanone **471** together with starting material (Table 9, entry 1). Even upon prolonged reaction times, full conversion was not achieved using these conditions (entry 2). At lower temperatures (entry 3), no product formation was observed. As a result, other acidic (entries 5, 6) and basic conditions (entry 6) were tested but afforded only similar product mixtures. Performing the cyclization using organocatalytic conditions (entry 7) led to full conversion of starting material but also to a lower isolated yield of the desired product. Finally, the cyclization attempt using benzylamine (entry 8) resulted only in decomposition of the starting material. The observation of the same ratio of starting material and product using various conditions indicated the formation of a thermodynamic equilibrium. This was confirmed by subjecting pure hydroxytwistanone **471** to the same reaction conditions resulting again in the same ratio as observed before. As it was possible to recycle the starting material, the yield of the overall transformation was raised to 75% by carrying out the cyclization reaction in several cycles. Thereby, hydroxytwistanone **471** was formed as a separable mixture of diastereomers in a ratio of about 7 : 1, according to NMR spectroscopy. A structural assignment of major and minor isomer was not possible at this stage.

Table 9. Screening of conditions for the aldol cyclization to generate the twistane core.



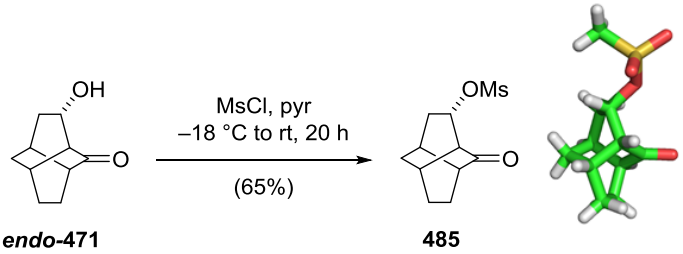
478 **471**

Entry	Reagent	Solvent	T [°C]	t [h]	Yield [%][a]	Ratio 478 : 471
1	HCl	acetone	56	3	39	~3 : 2
2	HCl	acetone	56	16	39	~3 : 2
3	HCl	acetone	rt	16	0	1 : 0
4	*p*-TsOH	PhH	60	3	35	~3 : 2
5	*p*-TsOH	PhH	80	3	35	~3 : 2
6	K_2CO_3	MeOH	65	3	37	~3 : 2
7	proline	DMF	rt	96	18[b]	0 : 1
8	benzylamine	THF	rt	16	-[c]	-

(a) Isolated yield. (b) Other products were formed but not characterized. (c) Formation of a multitude of products none of which could be characterized cleanly.

For the envisioned elimination of the secondary alcohol, hydroxytwistanone **471** was converted to its mesylate **485** (Scheme 108). Structural analysis of this species by single crystal X-ray diffraction

established the relative *endo*-configuration for the alcohol moiety of the major isomer of hydroxytwistanone **471**, in accordance with the observations by De Santis *et al*. in a related system.[201c]

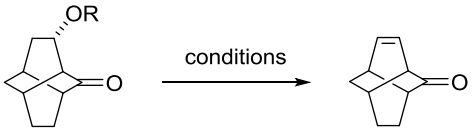


***endo*-471** **485**

Scheme 108. Conversion of ***endo*-471** to its mesylate **485**.

Unfortunately, attempts to effect the elimination using conditions which were reported for a closely related system only afforded decomposition of mesylate **485** (Table 10, entries 1, 2).[202] The use of other basic species did not lead to any observable reaction with the substrate, even at elevated temperatures (entries 3 to 7). In all of these cases it was possible to re-isolate the starting material.

Table 10. Attempts to eliminate the secondary alcohol using standard reagents.



***endo*-471**: R = H
485: R = Ms

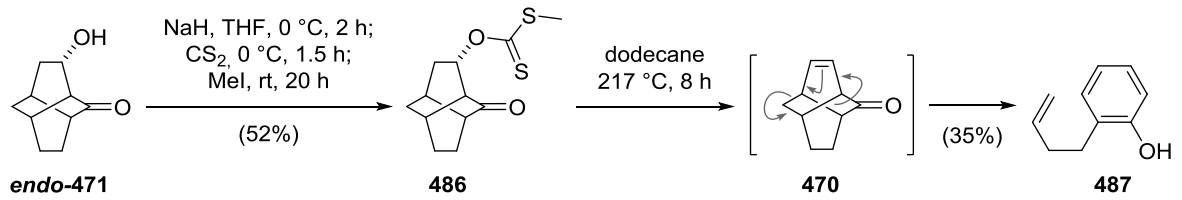
470

Entry	R	Reagent	Solvent	T [°C]	Observation
1	Ms	KO*t*-Bu	DMSO	60	decomposition
2	Ms	KO*t*-Bu	DMSO	rt	decomposition
3	Ms	DBU	$PhCH_3$	rt	no conversion
4	Ms	DBU	$PhCH_3$	60	no conversion
5	Ms	NaH	THF	rt	no conversion
6	Ms	NaH	THF	60	no conversion
7	Ms	NaH	PhH	80	no conversion
8	H	Burgess reagent	PhH	rt	no conversion
9	H	Burgess reagent	PhH	60	decomposition[a]
10	H	Burgess reagent	decane	170	decomposition[a]
11	H	Martin's sulfurane	CH_2Cl_2	rt	no conversion
12	H	Martin's sulfurane	CH_2Cl_2	40	no conversion

(a) Reaction monitoring by mass spectrometry and ^{1}H NMR spectroscopy showed the formation of an adduct of dehydrating agent and substrate but only a multitude of unidentified products was formed not containing any desired product.

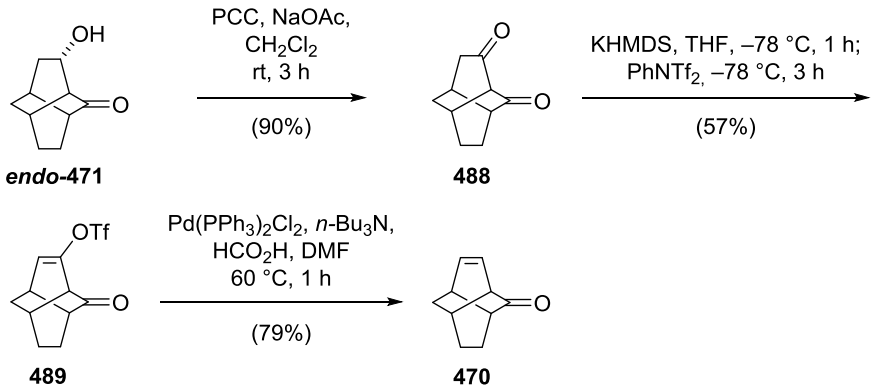
As all tested *anti*-elimination conditions proved futile, *syn*-elimination conditions using common dehydrating agents were investigated next. Thus, hydroxytwistanone ***endo*-471** was reacted with the Burgess reagent affording no conversion at room temperature (entry 8).[203] However, monitoring of reactions with the Burgess reagent at higher temperatures indicated the formation of an adduct with hydroxytwistanone ***endo*-471** but the desired product of elimination was never observed (entries 9, 10). In case of Martin's sulfurane, no conversion was achieved at room temperature as well as at higher temperatures and the starting material was recovered (entries 11, 12).

Next, hydroxytwistanone ***endo*-471** was converted to its xanthate **486** in order to perform a Chugaev elimination (Scheme 109). Indeed, upon heating a solution of xanthate **486** in decane to 170 °C it seemed as if traces of the desired twistenone **470** were formed. However, full conversion was not achieved. As a result, the elimination was conducted at an even higher temperature.[204] Due to the forcing conditions, a retro-Diels-Alder reaction followed by aromatization took place to afford phenol **487**.[205]



Scheme 109. Attempt to effect the elimination of the secondary alcohol using Chugaev's procedure.

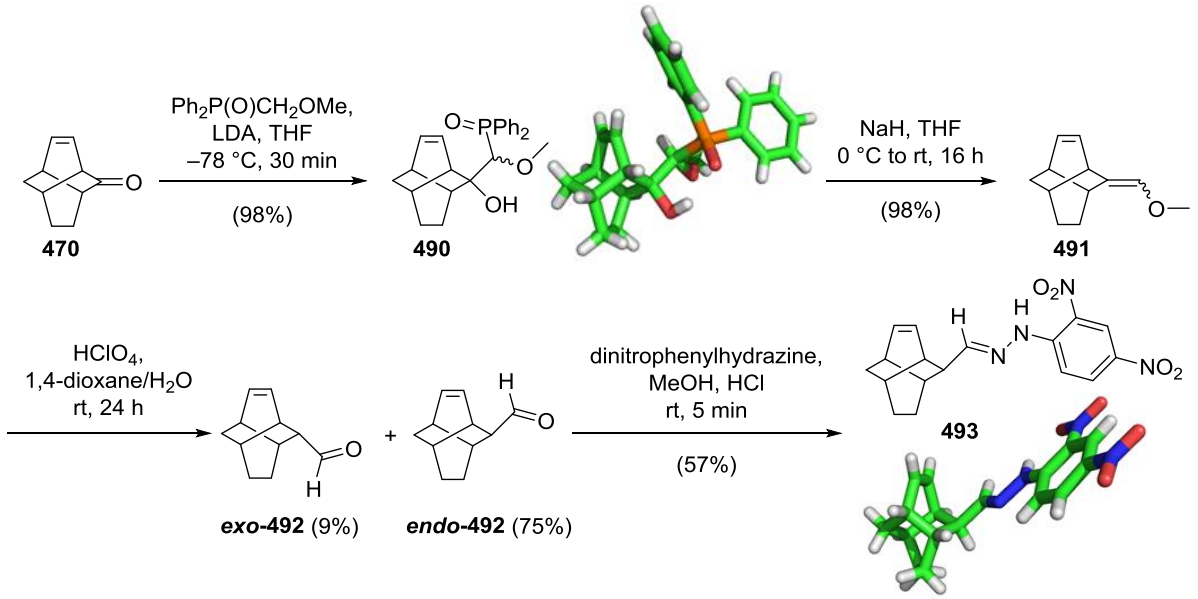
Therefore it was decided to introduce the double bond *via* a ketone. Oxidation of hydroxytwistanone ***endo*-471** provided diketone **488** which was selectively converted into enol triflate **489** (Scheme 110). As the enol triflation only returned a moderate yield, several reaction parameters were screened, including triflation reagent, order of addition and other additives but no marked improvement was achieved. Palladium-catalyzed reduction of enol triflate **489** gave the desired twistenone **470**.[206]



Scheme 110. Successful introduction of the double bond *via* ketone **488**.

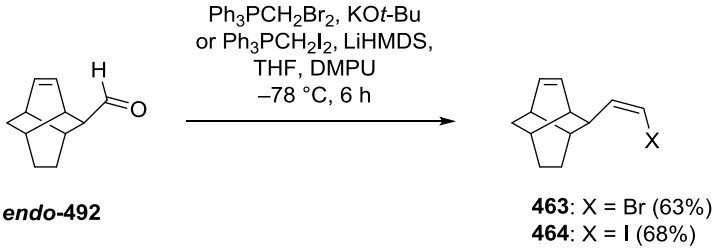
For the homologation of twistenone **470**, a three-step procedure devised by Warren and co-workers was used.[207] Addition of methoxymethyldiphenylphosphine oxide to twistenone **470** proceeded

selectively from the less hindered face but provided an inconsequential diastereomeric mixture of phosphine oxide **490** in regard to the methoxy group (Scheme 111).[208] Subsequent elimination of diphenyl phosphinate proceeded smoothly to afford enol ether **491** as an inconsequential (*E*)- to (*Z*)-mixture. Hydrolysis of the methyl enol ether under acidic conditions then gave carbaldehyde **492** as an 8 : 1 mixture of diastereomers in favor of the desired isomer ***endo*-492**. The diastereomers were separable by column chromatography and the configuration of the desired product was confirmed by single crystal X-ray diffraction after conversion to dinitrophenylhydrazone **493**.



Scheme 111. Homologation of twistenone **470** to aldehyde **492**.

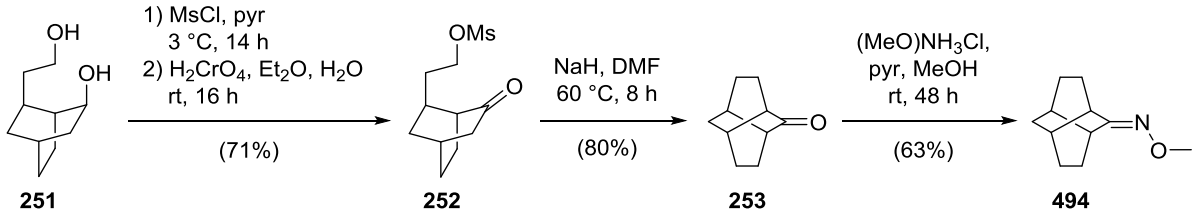
As for the bicyclic precursor compounds, the alkenyl halide functionality was established using Stork-Zhao reactions to afford alkenyl bromide **463** and alkenyl iodide **464** (Scheme 112).[180]



Scheme 112. Synthesis of alkenyl halides **463** and **464** *via* Stork-Zhao reactions.

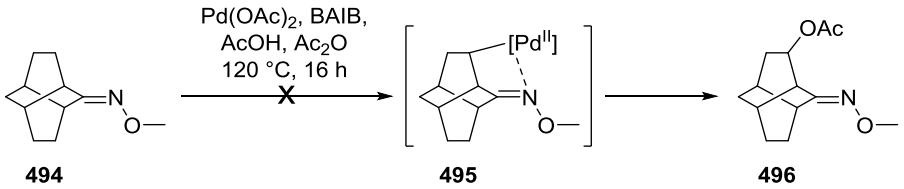
3.3.3 Attempts to Optimize the Synthetic Route to Twistenone 470

In order to enable a more efficient access to tricyclic precursor compounds **463** and **464**, ways to circumvent the problematic intramolecular aldol and enoltriflation step were investigated next. One possibility employing modern methodology was identified in the remote functionalization of twistanone oxime **494** *via* palladium-catalyzed C─H activation.[209] For this purpose, twistanone **253** was synthesized again following Whitlock's synthesis of twistane (**254**) (Scheme 113).[118] Thus, diol **251** was successively mesylated and oxidized to result in ketomesylate **252**. This compound was cyclized to twistanone **253** using an intramolecular enolate alkylation reaction. Finally, the oxime moiety was installed under basic conditions to provide oxime ether **494**.



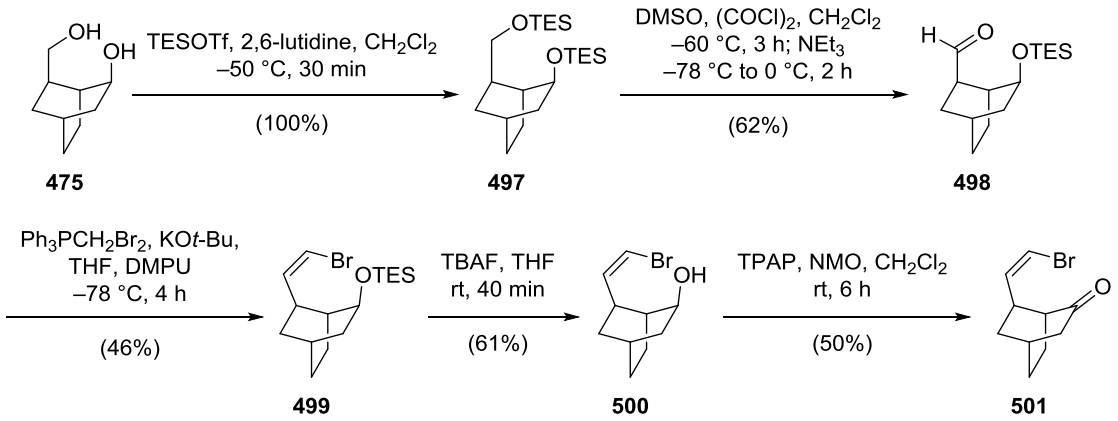
Scheme 113. Synthesis of oxime ether **494** as the precursor for C─H activation.

Subsequently, the envisioned directed C─H activation of oxime ether **494**, presumably occurring *via* an intermediate such as palladium complex **495**, was investigated (Scheme 114). However, using the reported standard conditions to effect the transformation did not provide any desired product. Increasing the reaction temperature and duration or conducting the reaction under pressure did not change the outcome of the reaction. Since not even traces of the desired product were found, the subsequent removal of the ketone protecting group is reported to be difficult[209b] and the enolate triflation step would still be necessary, other ways to optimize access to twistenone **470** were examined.



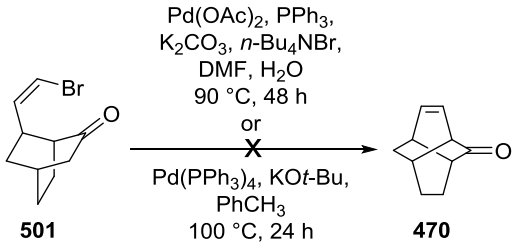
Scheme 114. Attempted C─H activation of oxime ether **494**.

An opportunity to bypass the aldol cyclization as well as the enoltriflation step would be to directly access twistenone **470** by an intramolecular enolate cross-coupling reaction of appropriately functionalized ketone **501** (Scheme 115).[210] In order to explore this route, diol **475** was doubly protected as bissilylether **497**. In an ensuing deprotective Swern reaction, the protected primary alcohol moiety was directly oxidized to result in carbaldehyde **498**.[211] Stork-Zhao olefination of this species then afforded alkenyl bromide **499**, which, after deprotection to alcohol **500**, was oxidized to the desired ketone **501**.



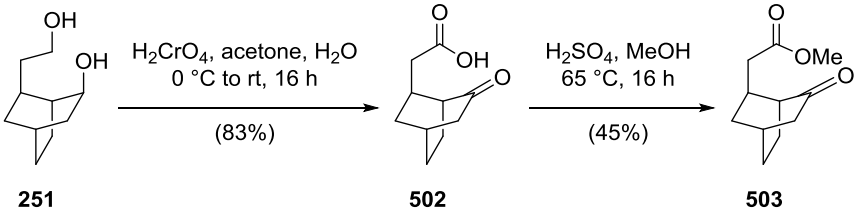
Scheme 115. Synthesis of ketone **501** as precursor for an intramolecular enolate cross-coupling reaction.

The cyclization of ketone **501** was attempted using two distinct conditions, which were successful in reports concerning similar systems (Scheme 116).[212] However, even elevated temperatures and prolonged reaction times did not afford conversion to the desired product. In the first case only decomposition of the starting material was found, whereas the second set of conditions did not afford any conversion. As this route did not promise to provide twistenone **470** in a better overall yield, due to drawbacks in the synthesis of the cyclization precursor, no exhaustive screening of conditions to accomplish the key step was executed.



Scheme 116. Attempted enolate cross-coupling reaction to form twistenone **470**.

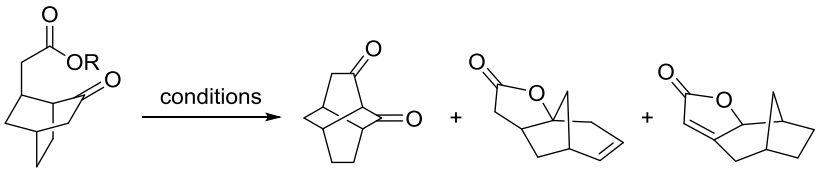
Another viable method to form the twistane core and thus avoid the aldol cyclization would be the Dieckmann-type condensation of keto acid **502** or keto ester **503** (Scheme 117).[213] Thus, known keto acid **502** was synthesized by Jones oxidation of diol **251**.[119b] Esterification of this species with methanol in sulfuric acid afforded methyl ester **503**.



Scheme 117. Synthesis of precursors **502** and **503** for a Dieckmann-type cyclization.

First, the cyclization was tested on keto ester **503** using acidic conditions.[214] Therefore, keto ester **503** was heated with *p*-TsOH resulting in decomposition of the starting material (Table 11, entry 1). In contrast, the use of CSA as proton source did not afford any observable conversion of the substrate (entry 2). Subsequently the transformation was also investigated employing basic conditions.[215] Whereas the reaction of keto ester **503** with KO*t*-Bu led to hydrolysis of the starting material (entry 3), no reaction was observed in the presence of HMDS bases and the starting material was re-isolated (entries 4, 5). Reacting keto ester **503** with LDA afforded after 1 h, according to GC-MS monitoring, partial conversion to the desired diketone **488**. After longer reaction times only products of decomposition were identified. Similarly, the reaction of keto acid **502** with different acidic dehydrating agents yielded no isolable product species (entries 7, 8, 9). Finally, heating a solution of keto acid **502** in Eaton's reagent furnished two products.[216] However, characterization by NMR spectroscopy revealed that novel tricyclic lactones **504** and **505** were formed instead of desired diketone **488**. In no case it was possible to isolate the desired product of the envisioned Dieckmann-type cyclization.

Table 11. Attempts to cyclize keto acid **502** and keto ester **503** using a Dieckmann-type reaction.[a]



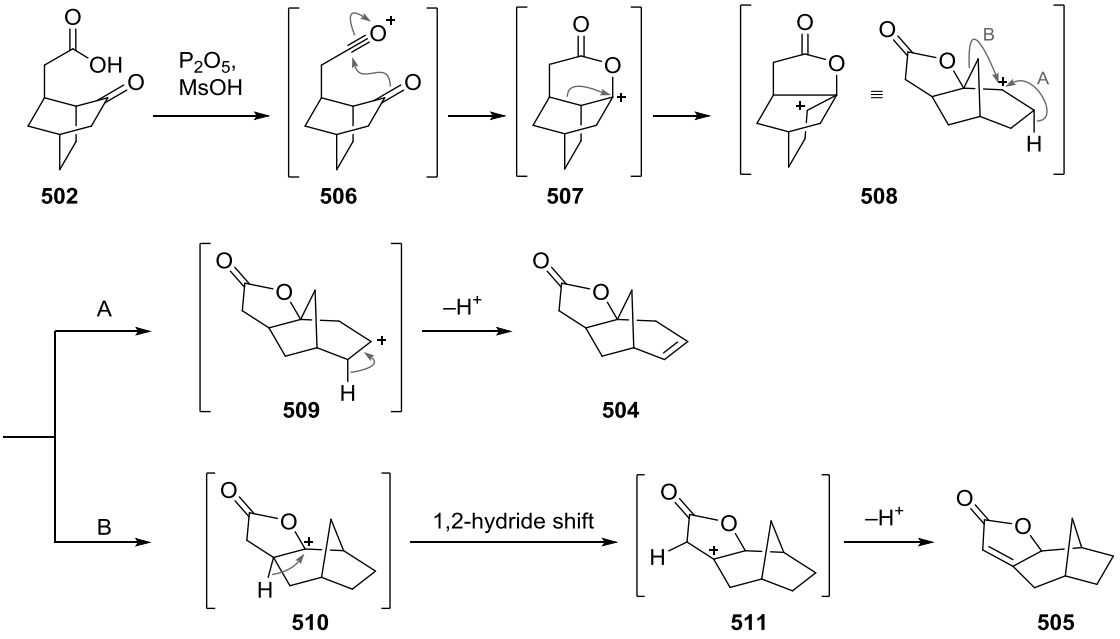
502: R = H
503: R = Me

488 **504** **505**

Entry	R	Reagent	Solvent	T [°C]	Observation
1	Me	*p*-TsOH	*m*-xylene	140	decomposition[b]
2	Me	CSA	*m*-xylene	140	no conversion[c]
3	Me	KO*t*-Bu	THF	40	hydrolysis
4	Me	KHMDS	THF	40	no conversion[c]
5	Me	NaHMDS	THF	40	no conversion[c]
6	Me	LDA	THF	40	decomposition[b,d]
7	H	PPA	AcOH	100	decomposition[b]
8	H	Ac_2O	Ac_2O	140	decomposition[b]
9	H	TFAA	TFA	70	decomposition[b]
10	H	Eaton's reagent	-	80	**504** + **505** (45%)[e]

(a) All reactions were either run until full conversion of starting material according to TLC and GC-MS or for 16 h if no conversion was observed. (b) Formation of a multitude of products none of which could be characterized cleanly. (c) According to GC-MS. Starting material was re-isolable. (d) After 1 h about 5% of the desired product was formed. To achieve higher conversion the reaction was continued but only afforded decomposition after 16 h. (e) **504** and **505** were reproducibly formed in a ratio of 1.4 : 1.

For the formation of rearranged lactones **504** and **505**, the following mechanism is supposedly operative (Scheme 118). Under the dehydrating acidic reaction conditions, the carboxylic acid moiety of keto acid **502** is converted to acylium ion **506**. In a nucleophilic attack of the ketone functionality, cationic lactone **507** is formed. In a subsequent Wagner-Meerwein rearrangement δ-lactone **507** is contracted to γ-lactone **508**. This species constitutes a branching point as two ensuing rearrangement pathways are possible. In one event (A), γ-lactone **508** undergoes a hydride shift resulting in cation **509** and then loses a proton to afford tricyclic lactone **504**. The other possibility (B) involves a Wagner-Meerwein-rearrangement to γ-lactone **510**. This then is followed by a hydride shift resulting in cation **511** which finally gets deprotonated to yield enone **505**. Although a variety of other rearrangement paths are imaginable, no further species were isolated from the reaction mixture.

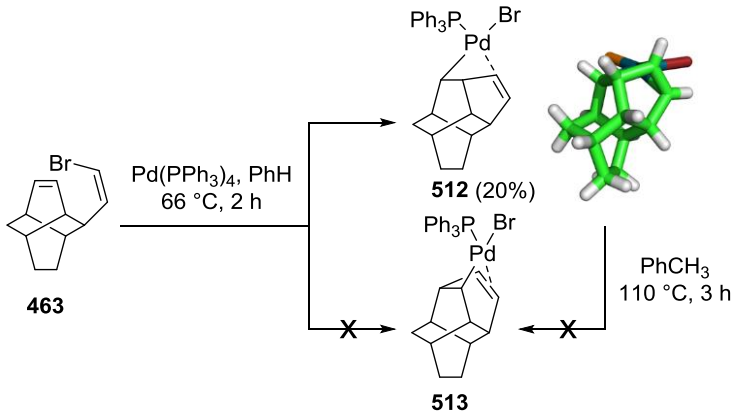


Scheme 118. Presumed mechanism for the formation of structurally interesting rearranged products **504** and **505**.

The attempts to optimize access to twistenone **470** provided the products of an interesting rearrangement but did not afford the desired species in a more efficient way. Therefore, it was decided to use the previously established synthetic route (see Chapter 3.3.2), which despite its drawbacks is able to deliver twistenone **470** on gram-scale.

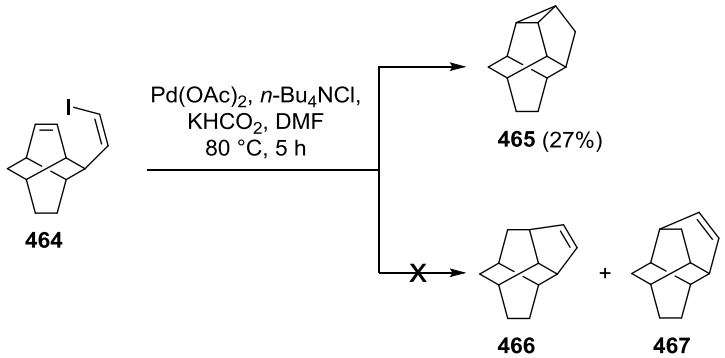
3.3.4 Cyclization Attempts of Tricyclic Precursors

With alkenyl halides **463** and **464** in hand, the crucial cyclization step was investigated again, using these presumably more biased systems. The first cyclization attempt was carried out employing stoichiometric amounts of $Pd(PPh_3)_4$ in order to facilitate the identification of the regiochemistry resulting from the cyclization. Indeed, crystals were obtained from the reaction of bromoalkenyltwistene **463** with the Pd(0)-source which proved suitable for single crystal X-ray diffraction. Disappointingly, the analysis of the X-ray structure showed that the undesired 5-*exo*-*trig* cyclization mode was operational to yield isoditwistene palladium complex **512** (Scheme 119). From the analogous reaction with iodoalkenyltwistene **464** only crystals of $PdI_2(PPh_3)_2$ were obtained. Attempts to thermally isomerize isoditwistene palladium complex **512** (corresponding to the less stable isomer **468**, Table 7, Chapter 3.2.4) to the desired ditwistene palladium complex **513** (corresponding to the more stable isomer **469**) proved unsuccessful and resulted in decomposition.



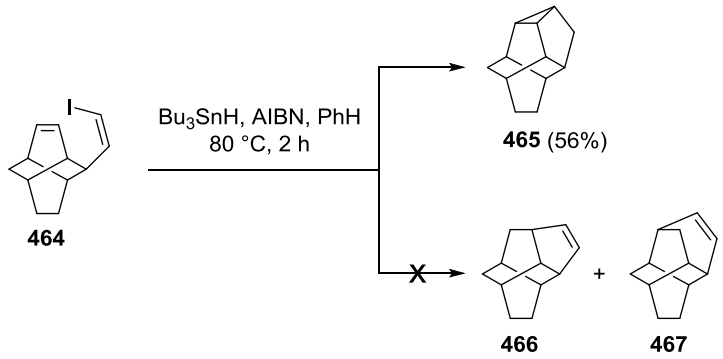
Scheme 119. Palladium-mediated cyclization of alkenyl bromide **463** and X-ray structure of isoditwistene palladium complex **512**. Phenyl rings are omitted for the sake of clarity.

Next, the cyclization was tested using reductive transition metal-catalyzed conditions (Scheme 120). All tested conditions gave cyclopropane **465**, a new hydrocarbon, as the only identifiable product, but failed to deliver the desired ditwistene **467** or even 5-*exo*-*trig* cyclization product **466**.



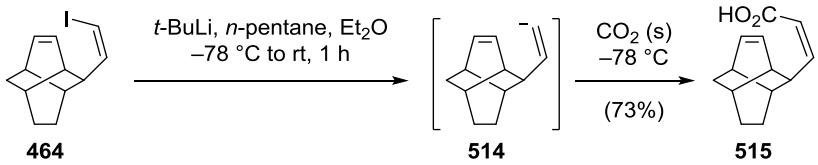
Scheme 120. Cyclization of alkenyl iodide **464** to cyclopropane **465** under reductive transition metal-catalyzed conditions.

In parallel to palladium catalysis, the cyclization was investigated employing reductive radical conditions. Again, only cyclopropane **465** was obtained and no olefinic species such as diisotwistene **466** or ditwistene **467** was observed (Scheme 121). Special attention was paid to the concentration of the reaction mixture, as the 5-*exo*-*trig* vs. 6-*endo*-*trig* selectivity of the radical reaction is reported to be sensitive to this parameter.[185b,c] Even when the reactions were run at concentrations as low as c = 0.01 M in substrate and Bu_3SnH, to allow for the establishment of the thermodynamic equilibrium, no formation of the desired product **467** was observed. Indeed, these experimental results reflect the thermodynamic stability of the hydrocarbon compounds, as predicted by computational chemistry (Table 6, Chapter 3.2.4.). It was found in these calculations that cyclopropane **465** might be the most stable of the three possible cyclized hydrocarbon compounds by an energy difference of 1.8 kcal·mol^{-1} in respect to the desired ditwistene **467**.



Scheme 121. Cyclization of alkenyl iodide **464** to cyclopropane **465** under reductive radical conditions.

In a further attempt to change the cyclization selectivity, alkenyl iodide **464** was submitted to carbolithiation conditions, thereby also simplifying the isolation and purification of the reaction products.[188] Therefore, metalation of alkenyl iodide **464** was carried out using *t*-BuLi followed by warming the reaction mixture to room temperature to allow for the cyclization to occur (Scheme 122). However, the only product found was carboxylic acid **515**, resulting from trapping of uncyclized carbanion **514**. The same outcome was observed if the reaction was warmed to 45 °C to enable the cyclization using a mixture of *n*-heptane and di-*n*-butylether as the solvent system. Interestingly, the product was found by analysis of the vicinal coupling constant to be exclusively in the (*Z*)-configuration indicating high configurational stability of intermediately formed carbanion **514**.[217]



Scheme 122. Cyclization attempt using carbolithiation conditions on alkenyl iodide **464**.

Like in the bicyclic system (see Chapter 3.2.3), atom transfer cyclization conditions were also investigated in order to achieve the desired 6-*endo*-*trig* cyclization (Table 12). However, submitting alkenyl bromide **463** to standard conditions for this transformation using CuBr as initiator resulted in the re-isolation of starting material (entry 1).[189] Upon irradiation of a solution of alkenyl iodide **464** in C_6D_6 in the presence of AIBN or Bu_6Sn_2,[190],[191] partial double bond isomerization was observed (entries 2, 3). As seen before, the ratio of (*Z*)- to (*E*)-isomer did not decrease below 3 : 1. The isomerization was established by the analysis of the relevant vicinal coupling constant from NMR spectroscopy (Figure 17). The shift of this value from $^3J_{C11\text{-}H,C12\text{-}H}$ = 7.2 Hz to $^3J_{C11\text{-}H,C12\text{-}H}$ = 14.4 Hz is a clear indication for the isomerization. An unambiguous characterization of the (*E*)-isomer was not possible due to the co-polarity of the species in (*Z*)- and (*E*)-configuration preventing purification of the newly formed species.

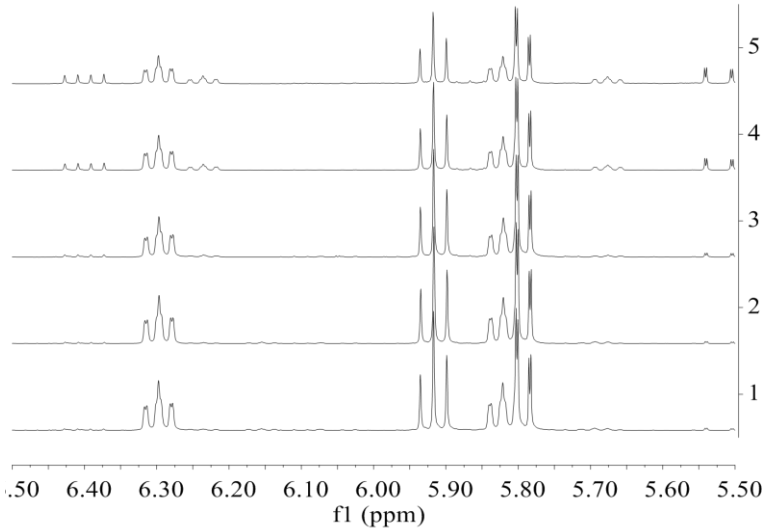
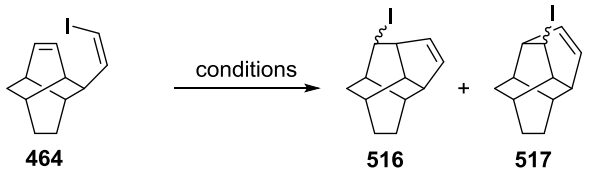


Figure 17. Comparison of the relevant range from ^{1}H NMR spectra of the attempted atom transfer cyclization: starting material (1), after addition of AIBN (2), after 2.5 h (3), 19 h (4) and 43 h (5) of irradiation.

Using another light source of higher intensity again afforded no conversion (entry 4). In an attempt to exploit the thermodynamics in a series of cyclization reactions, the initiator molecule **464** was also submitted to polymerization conditions using an excess of either methyl propiolate or 1-octyne as acetylene source. Neither thermal (entries 5, 6) nor photochemical conditions employing different solvents and light sources (entries 7 to 12) afforded polymeric materials, though. Despite the appearance of a purple color in the reaction mixtures, indicating an at least partial cleavage of the alkenyl iodide moiety, no significant mass increase was found after concentration of the reaction mixtures.[218] Indeed, it was possible to re-isolate substantial amounts of the starting material or identify it by ^{1}H NMR spectroscopy after the reaction.

Table 12. Screening of atom transfer cyclization and polymerization conditions to accomplish the desired 6-*endo*-*trig* cyclization.[a]



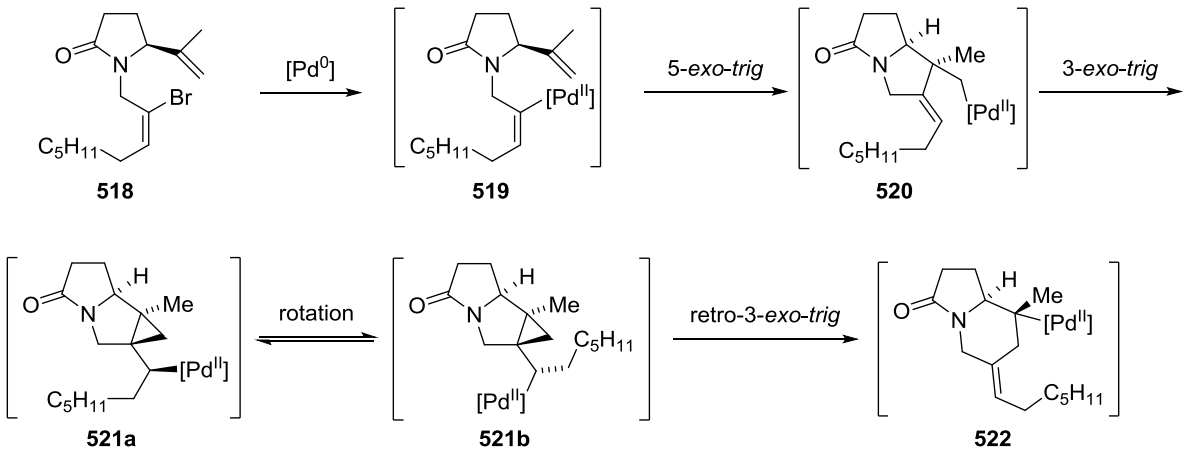
464 **516** **517**

Entry	Reagent	Monomer	Solvent	Irr. [W]	T [°C]	t [h]	Result
1[b]	CuBr	-	MeCN	-	110	16	no conversion
2[c]	Bu_6Sn_2	-	C_6D_6	275	50[d]	67	(*Z*)- to (*E*)- isom.[e,f]
3[c]	AIBN	-	C_6D_6	275	50[d]	67	(*Z*)- to (*E*)- isom.[e,f]
4[c]	Bu_6Sn_2	-	C_6D_6	450	rt	5	no conversion[e]
5	AIBN	propiolate	C_6H_6	-	80	16	no conversion[e,g]
6	AIBN	1-octyne	C_6H_6	-	80	16	no conversion[e,g]
7[h]	-	propiolate	C_6H_6	450	rt	4	no conversion[e]
8[h]	-	1-octyne	C_6H_6	450	rt	4	no conversion[e]
9	-	propiolate	*n*-hexane	450	rt	4	no conversion[e]
10	-	1-octyne	*n*-hexane	450	rt	4	no conversion[e]
11	-	propiolate	C_6H_6	275	50[d]	2	no conversion[e]
12	-	1-octyne	C_6H_6	275	50[d]	2	no conversion[e]

(a) All reactions were monitored by ^{1}H NMR spectroscopy. (b) Reaction was run in a sealed tube with alkenyl bromide **463** instead of alkenyl iodide **464**. (c) Reaction was performed in an NMR tube. (d) The temperature was a result of the position of the NMR tube distanced by 5 cm from the hot light source. (e) The reaction mixture changed color during the irradiation from colorless to purple. (f) According to analysis of the ^{1}H NMR spectra a 3 : 1 ratio of (*Z*)- to (*E*)-isomer was observed at the maximum. (g) Control reaction without alkenyl iodide **464** was run to identify side reaction of alkyne. (h) Reaction was run in pyrex flask as well as in a quartz tube.

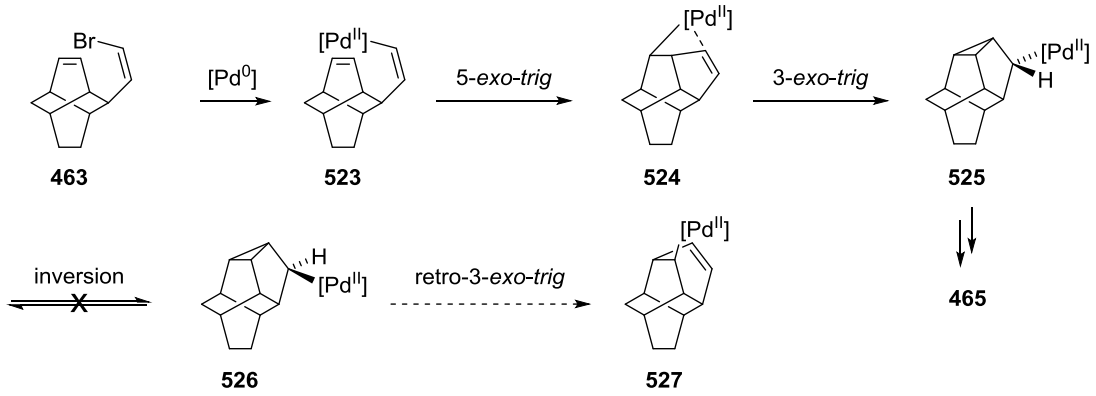
3.3.5 Discussion

It is well known that palladium-mediated cyclizations occur predominantly following the *exo*-mode for small to medium sized rings.[219] It has been argued that reported cases of *endo*-cyclizations in such systems actually take place in a sequence of two *exo*-cyclizations followed by a rearrangement.[220] This was proven for several substrates such as alkenyl bromide **518** (Scheme 123).[221] The mechanism for this transformation proceeds as follows: In a 5-*exo*-*trig* cyclization of oxidative addition product **519**, alkyl palladium complex **520** is formed. This homoallyl palladium complex is converted in a 3-*exo*-*trig* cyclization to cyclopropylcarbinyl palladium complex **521a**. After rotation about a single bond resulting in conformer **521b**, a retro-3-*exo*-*trig* cyclization to the apparent intermediate of a macroscopic 6-*endo*-*trig* cyclization **522** is possible.



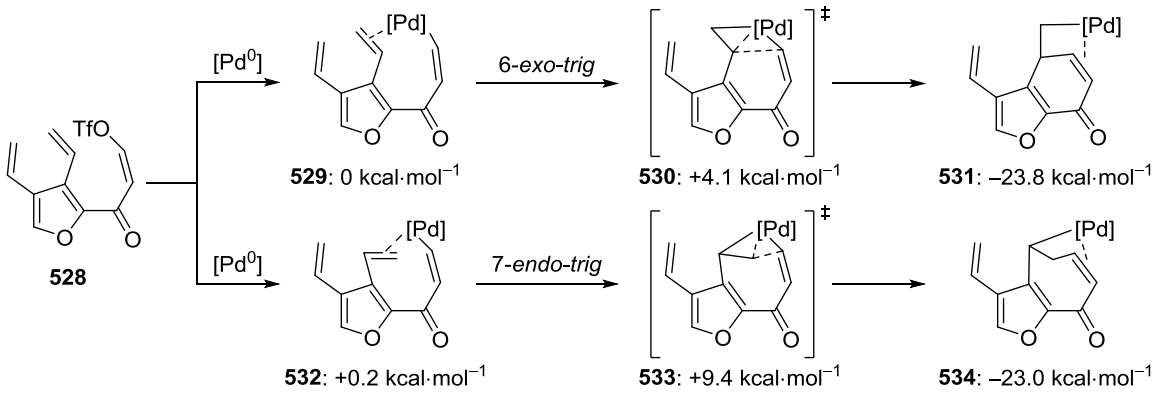
Scheme 123. Mechanism for the apparent palladium-catalyzed 6-*endo-trig* cyclization of alkenyl bromide **518**.

From three dimensional models it is obvious that this sequence of reactions is not possible for the present system because of its high rigidity. After consecutive 5-*exo-trig* and 3-*exo-trig* cyclizations of alkenyl palladium complex **523**, *via* homoallyl palladium complex **524**, cyclopropylcarbinyl palladium complex **525** would be formed (Scheme 124). The inversion of compound **525** to its diastereomer **526** cannot take place. Therefore, the ensuing rearrangement to ditwistene **527** is not possible and cyclopropane **525** is converted to the corresponding palladium hydride and undergoes reductive elimination to afford hydrocarbon **465** as observed in the catalytic reactions.



Scheme 124. Mechanism for the formation of cyclopropane **465**.

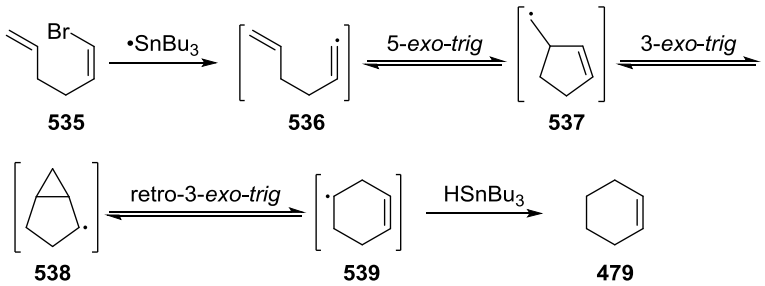
To explain the aforementioned empirical rule that palladium-mediated 6-*endo-trig* cyclizations do not occur, the geometry of the intermediates and transition states have to be considered. Previous computational studies showed that in a less strained system, like enol triflate **528**, the activation barrier for the 6-*exo-trig* cyclization *via* complex **529** and transition state **530** to cyclized complex **531** is favored by 5.3 kcal·mol^{-1} in respect to the competing 7-*endo-trig* cyclization, which proceeds *via* complex **532** and transition state **533** to cyclized complex **534** (Scheme 125).[222] These computational results are reflected in the experiment where the major product arises from formation of the 6-membered ring.



Scheme 125. Computational study of 6-*exo-trig* versus 7-*endo-trig* cyclization in system **528**.

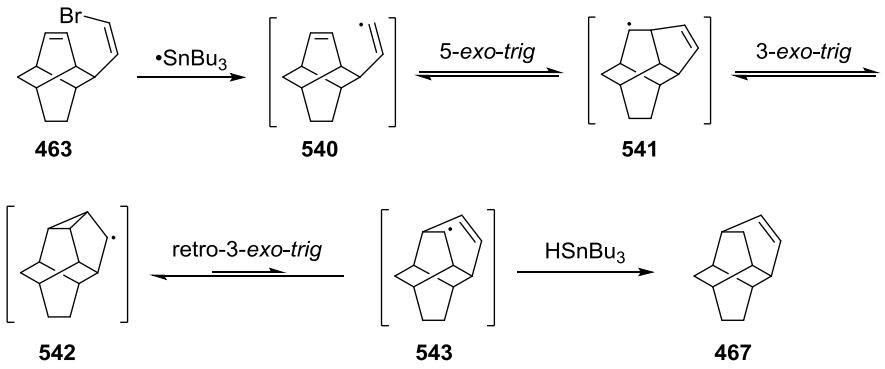
In calculations on the B3LYP/6-311+G(2d,p)/SDD level in the current system, no stationary point corresponding to the substrate of the 6-*endo-trig* cyclization was found, with all respective calculations converging on the substrate of the 5-*exo-trig* cyclization. This finding illustrates that the 6-*endo-trig* pathway is kinetically forbidden due to the necessary distortion of the alkenyl handle. Since the biasing conformational lock in the twistene system does not seem sufficient to compensate or lessen this strain, it can be concluded that palladium-catalyzed 6-*endo-trig* cyclizations in a 1-halo-1,5-diene system containing no heteroatom are in general kinetically not viable.

In radical chemistry, 5-*exo-trig* cyclizations occur very fast compared to 6-*endo-trig* cyclizations.[185b,c] However, in cyclizations involving vinyl radicals, the products of 5-*exo-trig* cyclization can interconvert to the product of the 6-*endo-trig* cyclization via a cyclopropylcarbinyl radical.[223] This mechanism was also investigated on acyclic 1-halo-1,5-diene **535** (Scheme 126). Vinyl radical **536**, which is formed from alkenyl bromide **535** upon radical abstraction, can cyclize *via* homoallyl radical **537** to cyclopropylcarbinyl radical **538**. After retro-3-*exo-trig* ring opening, cyclohexenyl radical **539** can be generated, which can be trapped to afford cyclohexene (**479**). Experimentally, the major products resulted from trapping of radical species **536** and **537**. Only traces of cyclohexene (**479**) were observed resulting from the trapping of radical **539**.



Scheme 126. Possible mechanism of an apparent 6-*endo-trig* radical cyclization of diene **535**.

For the configurationally more demanding twistene system **463** the corresponding mechanism is shown in Scheme 127. Therefore, vinyl radical **540** forms in a 5-*exo-trig* cyclization homoallyl radical **541**, which subsequently cyclizes to cyclopropylcarbinyl radical **542**. This would then need to open to homoallyl radical **543**, which then could be trapped to the desired ditwistene **467**. Unfortunately, cyclopropylcarbinyl radical **542** is the only species that is trapped by the tin hydride. However, this might be influenced by the introduction of radical stabilizing groups in appropriate positions on the twistane skeleton.



Scheme 127. Possible mechanism of an apparent 6-*endo-trig* radical cyclization in the twistene system.

The presented experimental and theoretical investigations lead to the conclusion that a "rational" approach to synthesizing polytwistane (**85**) from acetylene, as previously outlined, is unlikely to succeed. This does not preclude however, that polytwistane could be synthesized from acetylene under high temperature and / or high pressure conditions. It is also conceivable that fully saturated polytwistane could be made from the conducting polymer polyacetylene in its various forms.[167],[168]

3.4 Calculation of the NMR Chemical Shifts of Idealized Polytwistane

3.4.1 Computational Results Using Literature Data

To allow for the unambiguous characterization of polytwistane in complex reaction mixtures, calculations were performed to determine its ^{1}H and ^{13}C NMR spectrum. In the ideal polymer both spectra should consist of a single line due to its fascinating geometrical properties.[46] As a gradual approximation, the NMR spectra of several oligotwistanes of different length, $C_{20}H_{26}$ **291**, $C_{26}H_{32}$ **294**, $C_{32}H_{38}$ **401**, $C_{44}H_{50}$ **402** and $C_{46}H_{52}$ **403**, were calculated (Figure 18).

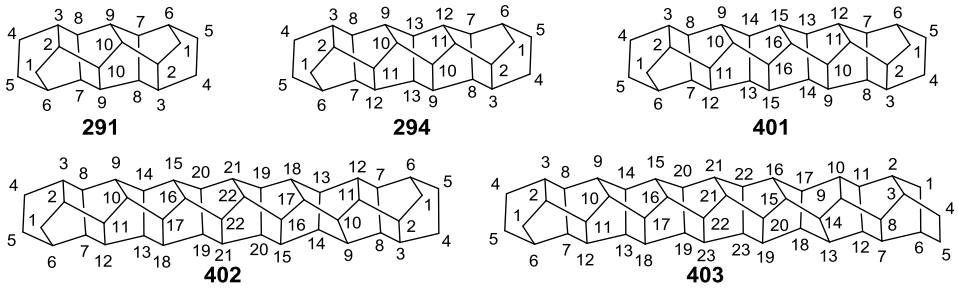


Figure 18. Structures of calculated oligotwistanes with atom numbering chosen so that increasing number corresponds to higher distance to the terminus.

Due to the rigidity of these systems no conformational analysis was undertaken since it was reasonable to assume that the geometry optimization provides the global minimum. All calculations were carried out using the B3LYP[193] density functional with the following basis sets: The 6-31G(d) basis set was used for geometry optimizations while the 6-31+G(d,p)[224] basis set was employed for the NMR calculations. The CPCM-SCRF implicit solvation method was used for treating solvent effects.[225] The GIAO approach was employed for the NMR calculations.[192],[226] For the conversion of calculated isotropic shielding to chemical shift values, the procedure developed by Tantillo was followed which uses a linear regression for reduction of systematic errors.[170b] Accordingly, the evaluation of the computational data for oligotwistanes **291**, **294**, **401**, **402** and **403** was performed using published values for the linear regression.[170b] In fact, a convergence of the chemical shifts of the methines was observed only for the larger oligotwistane **401**, **402** and **403**, reflecting the influence of the terminal methylenes (Figure 19 and Figure 20). Taking the average of the methines with an atom number higher than 14, the chemical shifts converge in the ^{1}H NMR to δ = 1.85 ppm and in the ^{13}C NMR to δ = 38.6 ppm. However, upon validation using several polycylic test compounds it was revealed that the reported scaling factors, which were used for the evaluation of the computational isotropic shielding, produced chemical shifts differing significantly from the experimentally observed values, especially in the ^{13}C NMR. This observation was attributed to the polycyclic nature of the test systems, since the set of compounds used to parametrize these scaling factors contains only a few polycyclic structures. Since polytwistane itself is highly polycyclic, taking this observation into account is of upmost importance. Furthermore, this finding is in accordance with the recent observations reported

by Andrews and Spivey,[227] that the accuracy of ^{13}C NMR shift prediction is greatly improved by taking recourse to similar chemical environments.

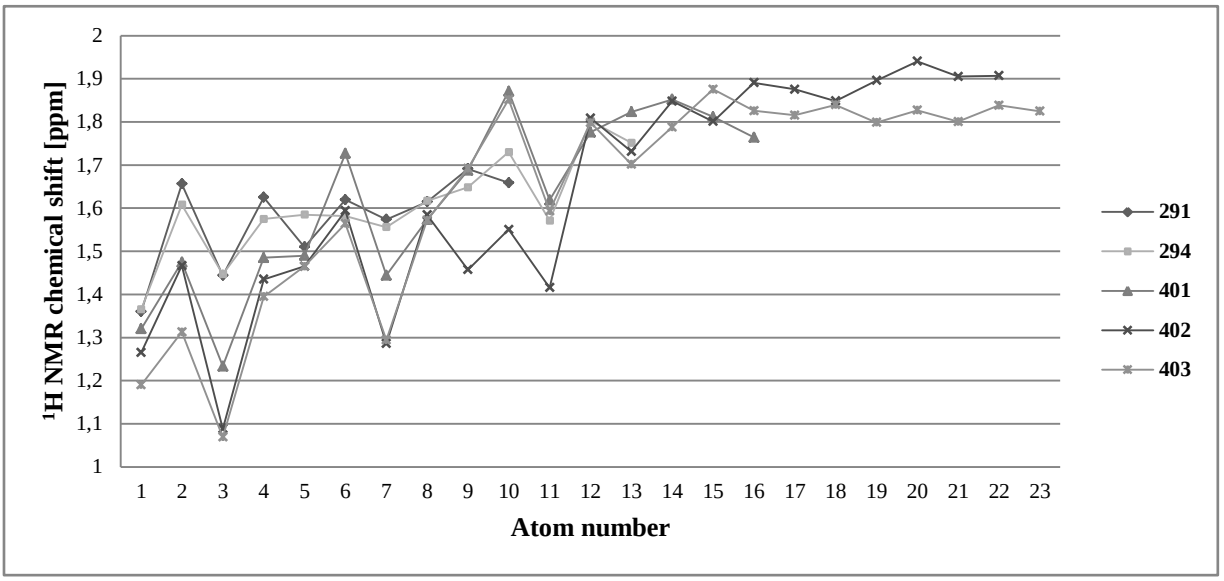


Figure 19. Calculated ^{1}H NMR chemical shifts of oligotwistanes **291**, **294**, **401**, **402** and **403** in dependence of the atom number as specified in Figure 18.

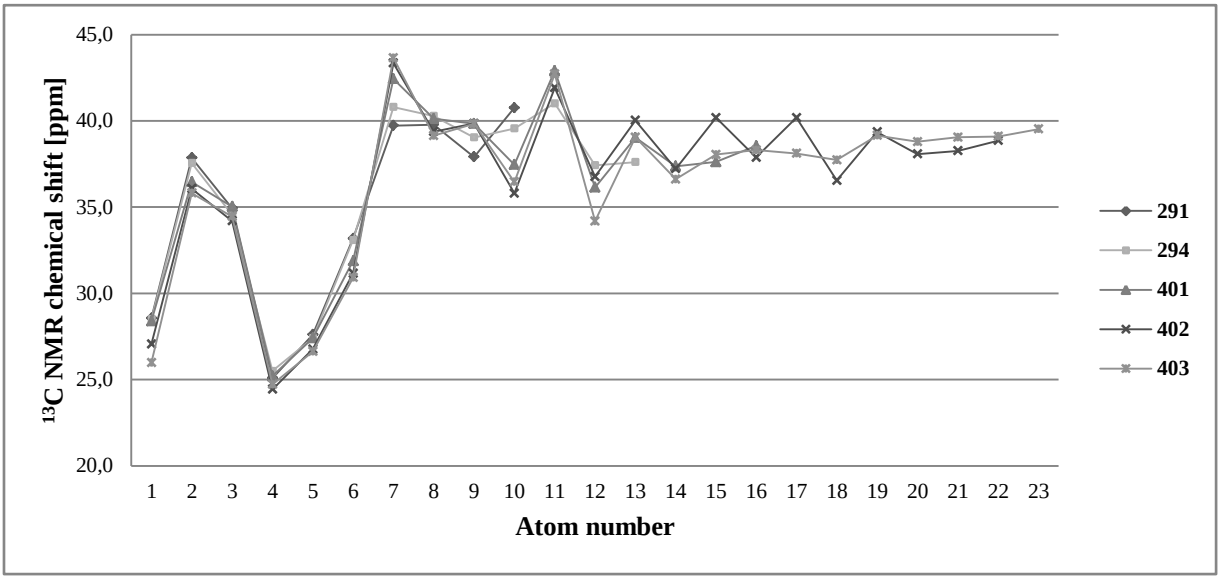


Figure 20. Calculated ^{13}C NMR chemical shifts of oligotwistanes **291**, **294**, **401**, **402** and **403** in dependence of the atom number as specified in Figure 18.

Subsequently, new scaling factors were to be established to achieve more accurate results.

3.4.2 Generation of New Scaling Factors – Synthesis of Reference Compounds

Experimental NMR chemical shifts for a range of relevant bi- to hexacyclic compounds were already available from the previously described work (Figure 21). Consequently, the NMR spectra of these molecules were calculated at the B3LYP/6-31+G(d,p)-CPCM-SCRF//B3LYP/6-31G(d) level so as to use them for the new linear regression scale.

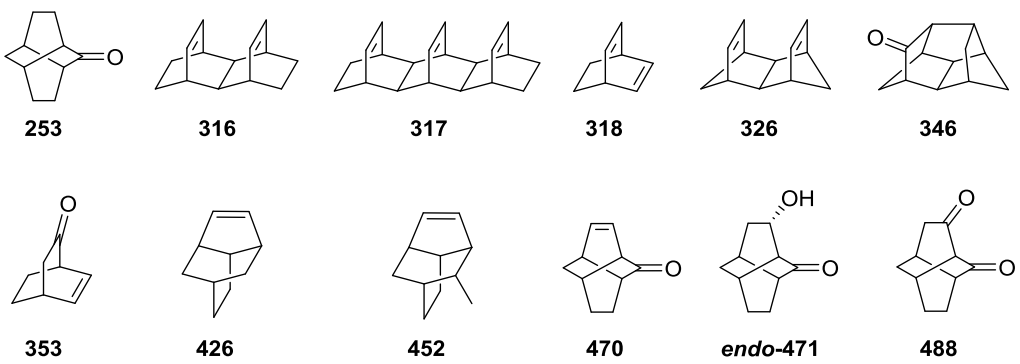
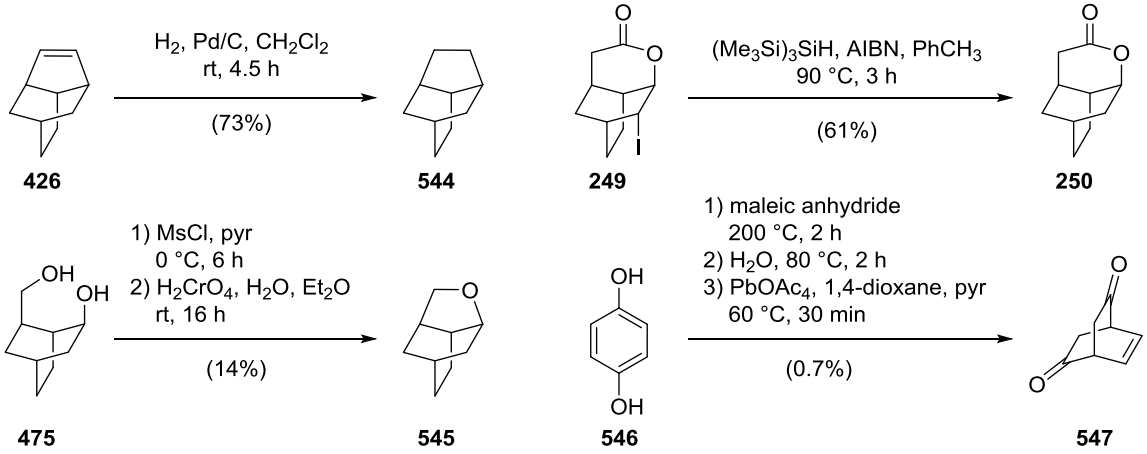


Figure 21. Available bi- to hexacyclic compounds from previous work.

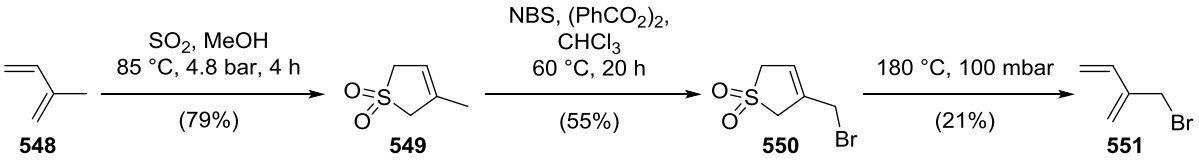
In order to obtain reliable scaling factors for the evaluation of polytwistane (**85**), a set of at least 20 polycyclic compounds was aimed for. Therefore, it was decided to first access some compounds by simple manipulations of available starting materials. Thus, isotwistene **426** was hydrogenated to isotwistane **544** (Scheme 128). Iodolactone **249** was deiodinated to known lactone **250** using a radical reductive procedure.[118],[228] Mesylation and subsequent cyclization of diol **475** gave rise to ether **545**. Bicyclooctadienone **547** was synthesized according to a literature procedure in three steps from hydroquinone (**546**) and maleic anhydride.[229]



Scheme 128. Synthesis of four bi- to tricyclic compounds to complement the test set for the new linear regression.

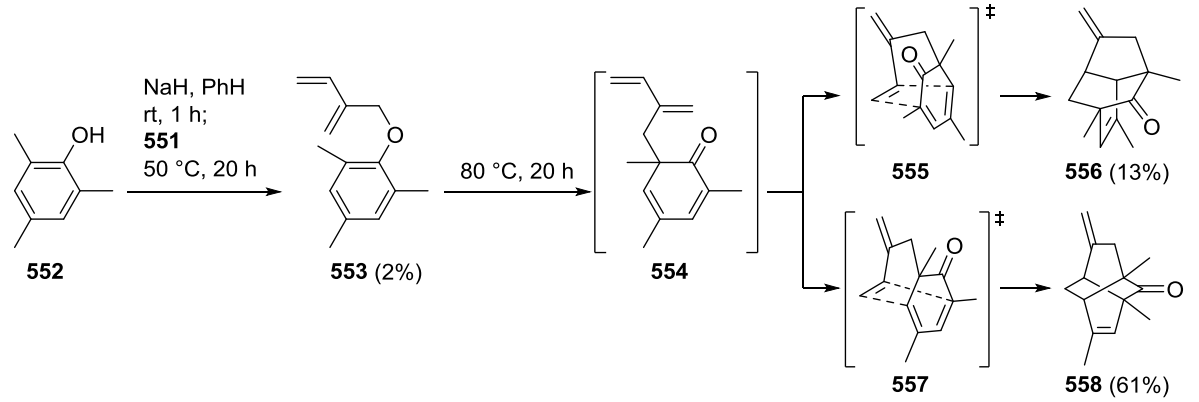
In addition, more compounds incorporating the twistane skeleton were synthesized, as they are expected to be ideally appropriate for the linear regression in light of the target of the computational study. For this reason, work reported by Greuter and Schmid furnishing fast access to the twistane

skeleton was reproduced and extended.[123] The starting material for this procedure, bromoisoprene **551**, was synthesized according to published procedures (Scheme 129). Thus, isoprene **548** was reacted in a cheletropic reaction with SO_2 to result in sulfolene **549**,[230] which was subsequently functionalized to yield bromosulfolene **550**.[231] Bromoisoprene **551** was then freshly prepared *via* flash vacuum pyrolysis of bromosulfolene **550** directly before its use in the next step.[232]



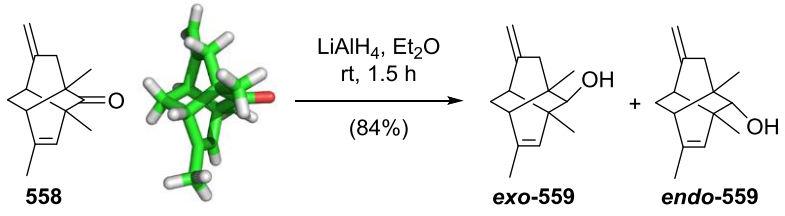
Scheme 129. Synthesis of bromoisoprene **551**.

The synthesis of isotwistene **556** and twistene **558** commenced with the allylation of phenol **552**, which afforded ether **553**. This was directly, by an increase of the reaction temperature, converted to tetraene **554** in a Claisen rearrangement. At the given reaction conditions, species **554** is only an intermediate and reacts in Diels-Alder reactions either *via* transition state **555** to isotwistene **556** or *via* transition state **557** to twistene **558**. Minor amounts of isoprenylether **553** were also isolated from the reaction mixture.



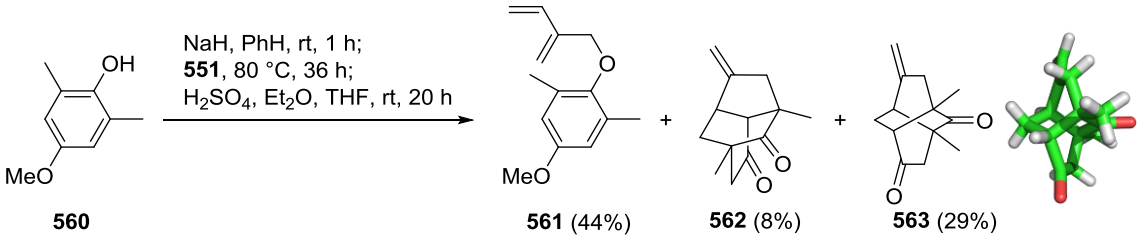
Scheme 130. Synthesis of isotwistene **556** and twistene **558**.

Ketone **558**, which displayed a pseudo C_2-axis in the structure obtained from single crystal X-ray diffraction, was reduced with $LiAlH_4$ to obtain the diastereomeric alcohols ***exo*-559** and ***endo*-559** (Scheme 131). Both were used for the parametrization of the new linear regression.



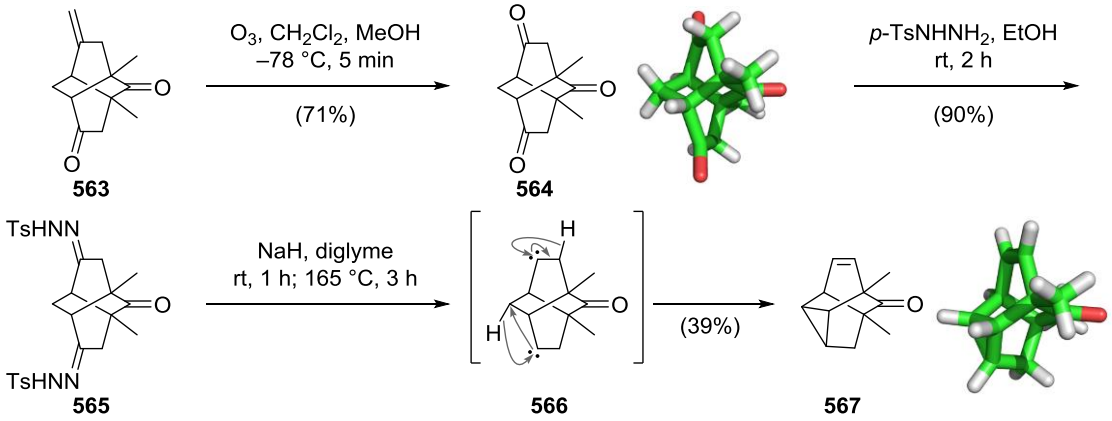
Scheme 131. X-ray structure and reduction of ketone **558**.

Easily accessible phenol **560** was reacted in an analogous allylation / Claisen rearrangement / Diels-Alder cascade to afford ether **561**, isotwistadione **562** and twistadione **563** (Scheme 132).[233] Ether **561**, which was obtained as the major product of this reaction, could be converted to the desired tricyclic products by heating in a high boiling unpolar solvent like decane.

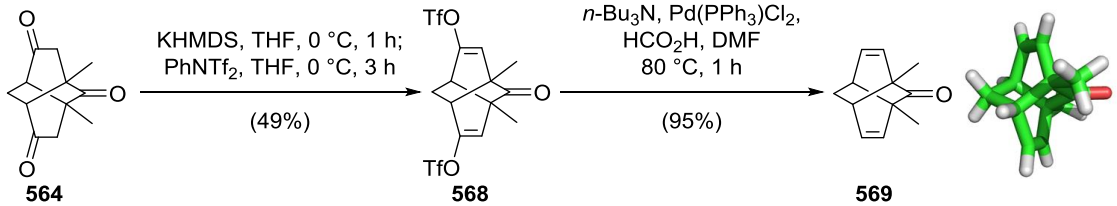


Scheme 132. Synthesis of isotwistene **562** and twistene **563**.

For further modification of twistadione **563** it was planned to introduce two double bonds on the ethylene bridges using the Shapiro olefination. Thus, ozonolysis gave rise to C_2-symmetric trione **564**, which was subsequently transformed to bistosylhydrazone **565** (Scheme 133). As attempts to effect the planned Shapiro olefination with LDA, *n*-BuLi or *t*-BuLi resulted only in the re-isolation of starting material,[234] the olefination next was tried using Bamford-Stevens conditions.[235] However, under these conditions only the formation of cyclopropanene **567**, which is presumably formed by a hybrid [1,2] and [1,3] carbene C─H insertion of dicarbene **566**, was observed. The structure of cyclopropanene **567** was unambiguously proven by single crystal X-ray diffraction.



Scheme 133. Further modification of dione **563** leading to cyclopropanene **567**.



Scheme 134. Synthesis of diene **569** *via* reduction of enol triflate **568**.

For the generation of the envisioned diene species **569**, the alternative established procedure for the reduction of enol triflates was effective. Therefore, trione **564** was converted to its bisenol triflate **568**, which was subsequently catalytically reduced to the desired diene **569** (Scheme 134).

Consequently, from the experimental and computational NMR data from the test set of 25 compounds which contain bi- to hexacyclic scaffolds, a new linear regression was parametrized (see Figure 37 for an overview of all test compounds). The plots for the linear regressions and the resulting lines of best fit are displayed in Figure 22 for ^{1}H NMR and in Figure 23 for ^{13}C NMR.

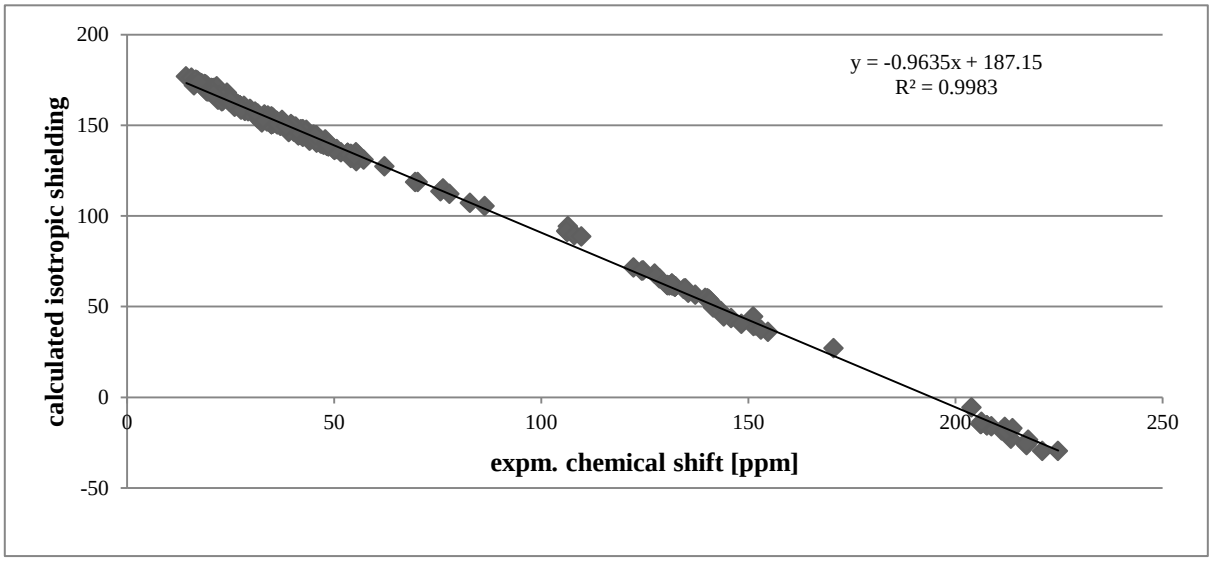


Figure 22. New linear regression for ^{1}H NMR using the B3LYP/6-31+G(d,p)-CPCM-SCRF//B3LYP/6-31G(d) level with the formula for the line of best fit. R^2 = coefficient of determination.

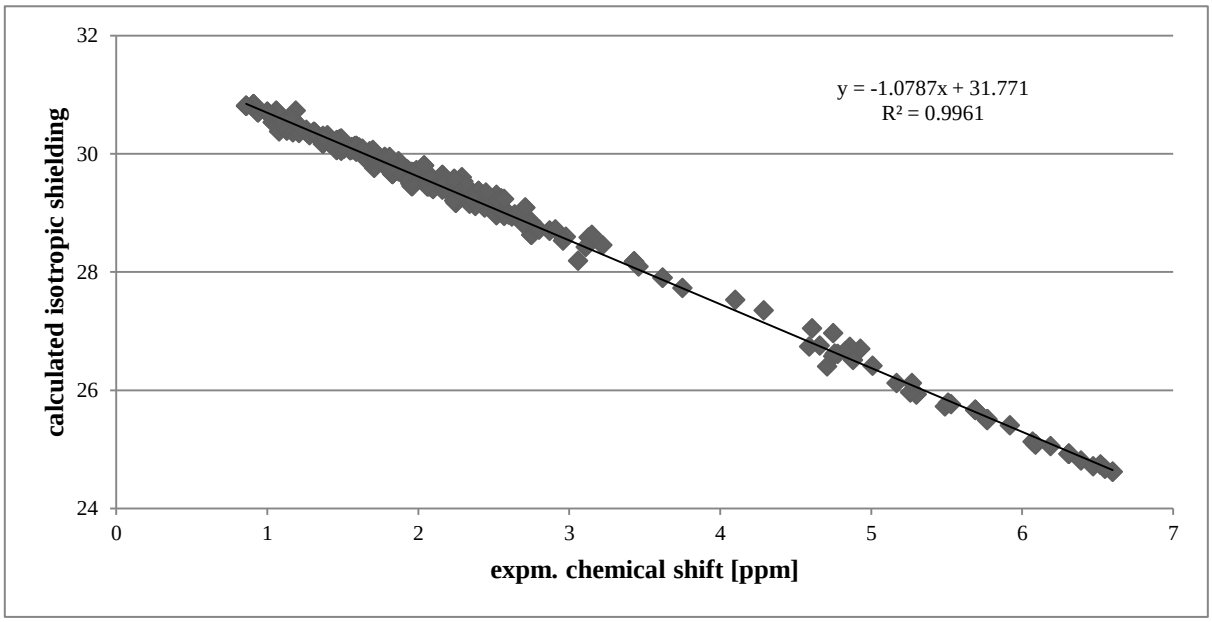


Figure 23. New linear regression for ^{13}C NMR using the B3LYP/6-31+G(d,p)-CPCM-SCRF//B3LYP/6-31G(d) level with the formula for the line of best fit. R^2 = coefficient of determination.

As apparent from the comparison of the published scaling factors and the new scaling factors (Table 13), the difference is marginal for ^{1}H NMR, but the disagreement for the ^{13}C NMR shifts amounts to almost δ = 3.0 ppm.

Table 13. Reported values for slope and intercept for the computational method B3LYP/6-31+G(d,p)-CPCM-SCRF//B3LYP/6-31G(d) compared to values obtained from the test set of bi- to hexacyclic compounds.

NMR nucleus	Value	Generic Test Set[a]	Polycyclic Test Set
^{1}H	slope	−1.0472	−1.0787
	intercept	31.6874	31.771
^{13}C	slope	−0.9600	−0.9635
	intercept	190.0155	187.150

(a) As reported by Tantillo.[170b]

As a validation for these linear regression values, the computational and experimental data for C_2-tritwistane (**288**) were compared and resulted in a standard deviation of δ = 0.06 ppm for its ^{1}H NMR spectrum and δ = 1.43 ppm for its ^{13}C NMR spectrum.

3.4.3 Computational Results Using New Scaling Factors

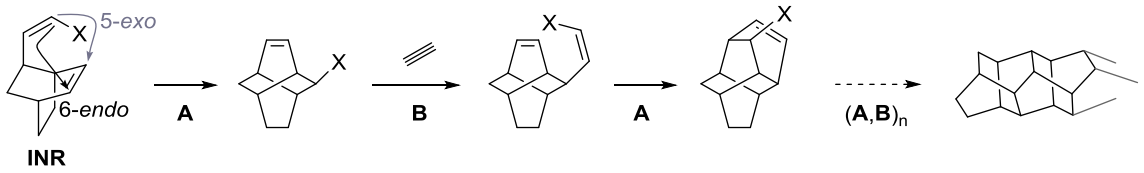
As a result, the evaluation of the computational data for oligotwistanes **291**, **294**, **401**, **402** and **403** was repeated using the new scaling factors. The results show convergence of the chemical shifts in ^{1}H NMR to δ = 1.85 ppm and in ^{13}C NMR to δ = 35.5 ppm. Assuming that the chemical environment of the methines does not change significantly in going to the ideal polymer, these chemical shifts represent the values expected for infinite polytwistane.

Alternatively, a more elaborate non-empirical quantum chemical approach was performed in cooperation with the group of Prof. Ochsenfeld (Ludwig Maximilian University, Munich), for the large systems using recently developed linear scaling NMR methods.[236] This approach exploits a higher level of theory and was chosen after comparison of various computational methods, including CCSD calculations for an intermediate reference.[237] In ^{1}H NMR a distinct difference of $\Delta\delta$ = 0.43 ppm (23% deviation) was observed, which is attributed to the independence of this approach from the experimental data. In ^{13}C NMR all methods show close accordance with an absolute difference of $\Delta\delta$ = 2.2 ppm (7%).

Overall, the most reliable computed data predicts the NMR chemical shifts of polytwistane to be δ = 1.5 ppm for ^{1}H and δ = 33 ppm for ^{13}C NMR.[238] Thus, the identification of polytwistane should be considerably simplified.

3.5 Conclusion and Future Directions

In this part, a possible synthetic access to polytwistane (**85**) was outlined and pursued. For this purpose, an acetylene polymerization was devised which was envisioned to be structurally governed by a suitable bicyclic or tricyclic initiator compound **INR** (Scheme 135).



Scheme 135. Proposed acetylene polymerization for the synthesis of polytwistane (**85**).

To investigate the planned transition metal-catalyzed or radical polymerization, bicyclic and tricyclic precursors were successfully synthesized on scale. Thus, bicyclic alkenyl bromides **418**, **438**, **439** and **440** were accessed in subsequent Diels-Alder and Stork-Zhao reactions (Figure 24).[178]

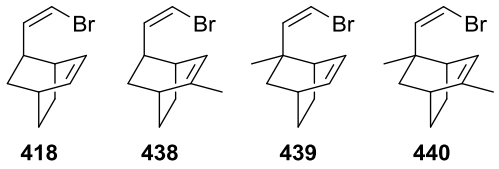
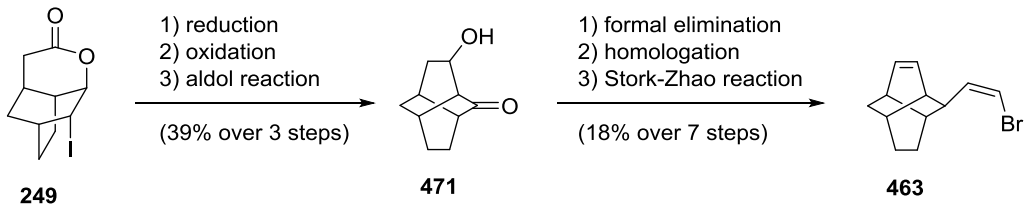


Figure 24. Bicyclic initiator compounds.

For the synthesis of tricyclic precursor **463** a reliable and scalable synthetic route commencing with known iodolactone **249** was developed (Scheme 136).[118] An intramolecular aldol reaction was used for the generation of the twistane framework, followed by elimination of the resulting hydroxyl moiety *via* reduction of an enol triflate. The alkenyl bromide handle was finally installed by homologation of the ketone moiety and subsequent Stork-Zhao olefination.



Scheme 136. Synthesis of tricyclic precursor **463**.

The regioselectivity of the crucial cyclization step (5-*exo*- vs. 6-*endo*-*trig*) was studied with all available precursor compounds using transition metal catalysis as well as radical conditions. During these investigations, several interesting hydrocarbon compounds and palladium complexes were obtained (Figure 25). The latter were characterized standardly by single crystal X-ray diffraction allowing an unambiguous assignment of the observed regiochemistry. Unfortunately, it was found that all observed products were formed by the undesired 5-*exo*-*trig* cyclization mode. This observation was

also supported by studies using computational chemistry, which showed that the desired 6-*endo-trig* cyclization by transition metal catalysis is impossible due to geometric constraints. Thus, a polymerization leading to polytwistane (**85**) was not yet achieved.

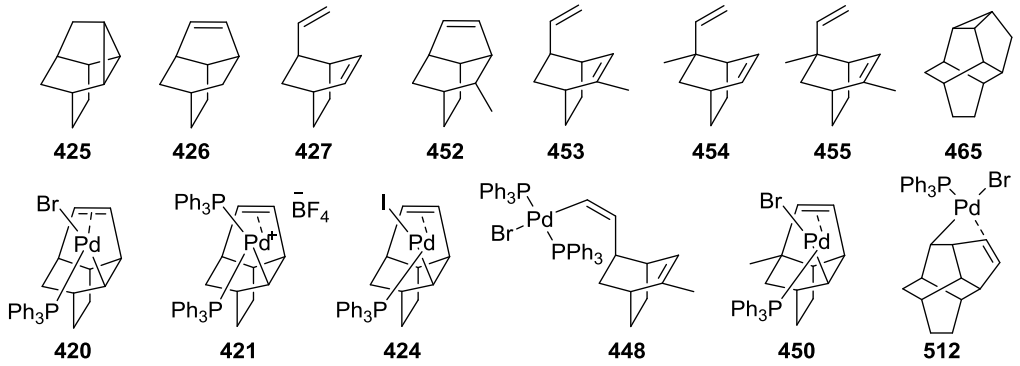
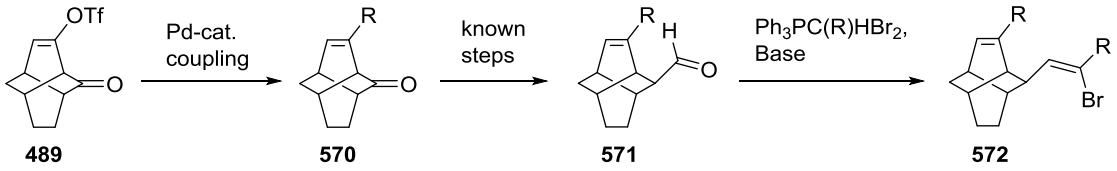


Figure 25. Products resulting from attempts to enable the critical cyclization step.

To allow for the identification of polytwistane (**85**) from complex reaction mixtures, the NMR properties of ideal polytwistane (**85**) were calculated. The calculations made use of a linear regression scheme on oligomers as large as $C_{46}H_{52}$.[170b] Convergence of the chemical shifts with increasing distance to the termini was observed, resulting in an expected ^{1}H NMR chemical shift of δ = 1.5 ppm and ^{13}C NMR chemical shift of δ = 33 ppm for the ideal polymer. Interestingly, these values are in close accordance with the experimental data found for the central methine unit of C_2-tritwistane (**288**) (δ = 1.48 ppm and δ = 35.4 ppm respectively).

In the future, the focus will be put on facilitating the radical pathway to polytwistane (**85**). In this regard, the introduction of radical stabilizing groups on the positions crucial for the polymerization might be beneficial (Scheme 137). This could be done for example by palladium-mediated functionalization of enol triflate **489** and subsequent olefination using modified Stork-Zhao reagents.



Scheme 137. Proposed functionalization of the tricyclic initiator compound to facilitate the formation of polytwistane (**85**) in a radical polymerization (R = Me, CO_2Me, CN, NO_2, Ph).

Additionally, other possible approaches to polytwistane (**85**) using non-standard conditions like high temperature and / or high pressure still have to be explored. In this context it has to be mentioned that fully saturated polytwistane could be made from the conducting polymer polyacetylene in its various forms.

4 Synthesis of Twistanamines

4.1 Background and Aims

Adamantane (**573**), the stabilomer of $C_{10}H_{16}$, displays a similarly rigid but completely unstrained cage due to its cyclohexane rings being in the chair conformation (Figure 26).[239] The resulting stability together with its availability, physical properties and geometric characteristics led to its extensive use in medicinal chemistry.[240] The pharmaceutical functions of the adamantane building block are various and include the use as a modulator for adsorption, distribution, metabolism and excretion chararacteristics. Additionally, the adamantane cage is utilized as a lipophilic ligand, as a disruptor of transmembrane flow and as a rigid three-dimensional scaffold for other functionalities.[240a] As a result, several top-selling drugs containing the adamantane motif are currently on the market (Figure 26). The diseases they are used against range from Alzheimer which can be treated with memantine (**574**) over diabetes which can be controlled with saxagliptin (**575**) to cancer for which the use of adaphostin (**576**) is studied.

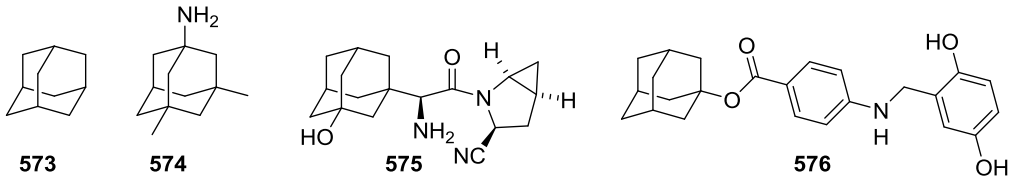


Figure 26. Structure of adamantane (**573**) and some pharmaceuticals containing the adamantane scaffold.

However, the first medicinal application of an adamantane derivative, amantadine (**577**), was against influenza A virus (Figure 27).[241] This was found shortly after adamantane (**573**) was made available on large scale by the seminal synthesis of Schleyer.[242] In recent years the mode of action of amantadine (**577**) was elucidated by co-crystallization with its target. Thus, it was shown that amantadine (**577**) blocks the proton flow through the M2 ion channel of influenza A virus *via* a "cork in the bottle" mechanism and therefore inhibits the uncoating of the viral genom.[243]

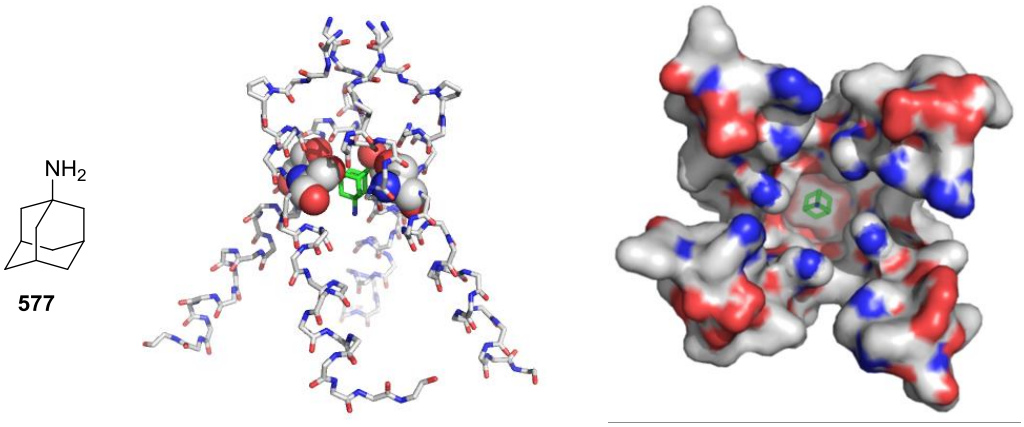


Figure 27. Amantadine (**577**) and models of amantadine (**577**) blocking the M2 ion channel of influenza A virus (PDB: 3C9J).[243]

Due to mutations in the conserved binding site of the M2 ion channel, the influenza A virus today has achieved almost 100% resistance against classic adamantane derived drugs.[244] Therefore, the search for alternatives gains importance.[245] In this regard, the structural similarity of adamantane and twistane is of particular interest (Figure 28) and resulted in the patenting of twistanamine **578** as an antiviral agent already in 1971.[246]

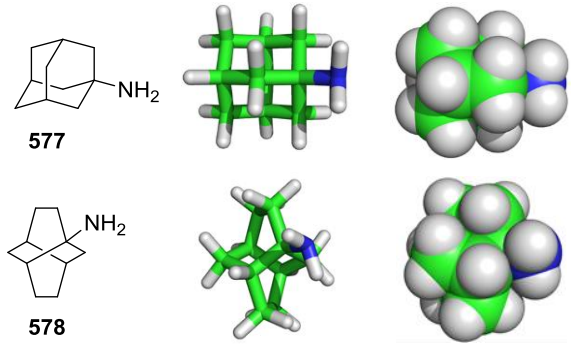


Figure 28. Structural similarity between amantadine (**577**) and twistanamine **578** visualized with three-dimensional models.

Twistane (**254**) presents several interesting features for an application as a framework for novel antiviral agents. On one side, it shows properties similar to adamantane (**573**) and analogously may be used as a three-dimensional scaffold but on the other side offers different orientations of the ligands. Additionally, it has a slightly different shape than adamantane (**573**), which might be of importance for activity against influenza A virus mutants, which display resistance against adamantane derived drugs. Also, owing to its molecular point group (D_2), twistane (**254**) is chiral and thus offers a new aspect to the synthesis of potential drugs. For these reasons, it was decided to synthesize twistanamines **579** to **584** and test them for their biological activity against influenza A virus mutants (Figure 29).

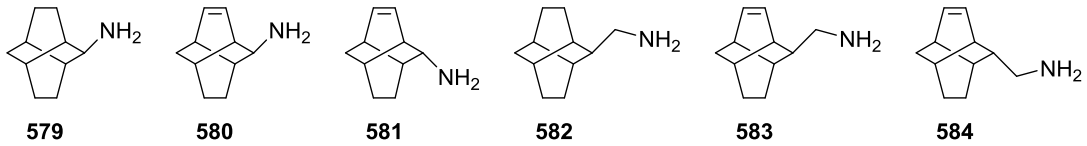


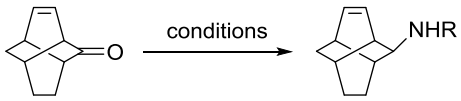
Figure 29. Twistanamines planned to be synthesized and tested for their biological activity.

4.2 Synthesis of Twistanamines

4.2.1 Twistanamines

In order to access the desired twistanamines **579** to **581**, the amination of twistenone **470** was investigated first (Table 14). Thus, twistenone **470** was submitted to conditions which were reported to provide primary amines.[247] However, at the usual temperature for this transformation, as well as at elevated temperatures, no reaction was observed and the starting material was recovered from the reaction mixture (entries 1, 2). The same outcome resulted from an attempt using standard amination conditions (entry 3). Also, the use of ammonia equivalents (entries 4, 5, 6) was not successful.[248] These observations were attributed to the high steric demand at the ketone functionality and thus presumably required more reactive species.

Table 14. Attempts to synthesize twistanamines by amination of twistenone **470**.[a]



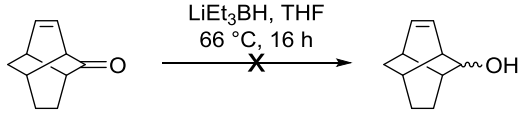
470

580: R = H
585: R = Trt
586: R = Bn

Entry	R	Reagents	Solvent	T [°C]	Result
1	H	NH_4Cl, $NaBH_4$, $Ti(O\textit{i}\text{-}Pr)_4$, NEt_3	EtOH	rt	no conversion
2	H	NH_4Cl, $NaBH_4$, $Ti(O\textit{i}\text{-}Pr)_4$, NEt_3	EtOH	78	no conversion
3[b]	H	NH_4OAc, NH_3, $NaBH_3CN$	EtOH	90	no conversion
4	Trt	$TrtNH_2$, 4 Å MS, $NaBH_3CN$	MeOH	65	no conversion
5[b]	Trt	$TrtNH_2$, 4 Å MS, $NaBH_3CN$	EtOH	100	no conversion
6[b]	Bn	$BnNH_2$, 4 Å MS, $NaBH_3CN$	EtOH	100	no conversion

(a) All reactions were carried out for at least 48 h. (b) Reaction was carried out in a pressure tube.

Next, twistenone **470** was to be reduced to twistenol **587** to enable the introduction of the amine functionality by a nucleophilic displacement. However, twistenone **470** resisted reduction even upon treatment with $LiEt_3BH$ in refluxing THF (Scheme 138).

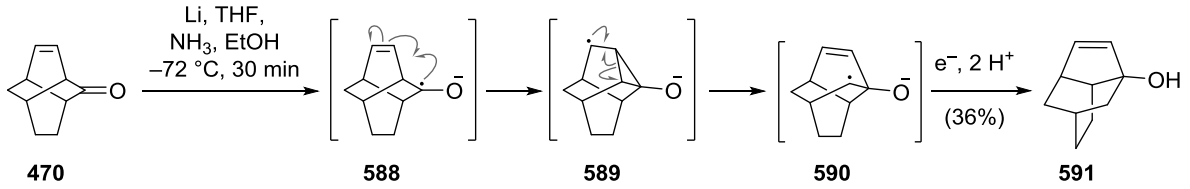


470 **587**

Scheme 138. Attempt to reduce twistenone **470** using hydride sources.

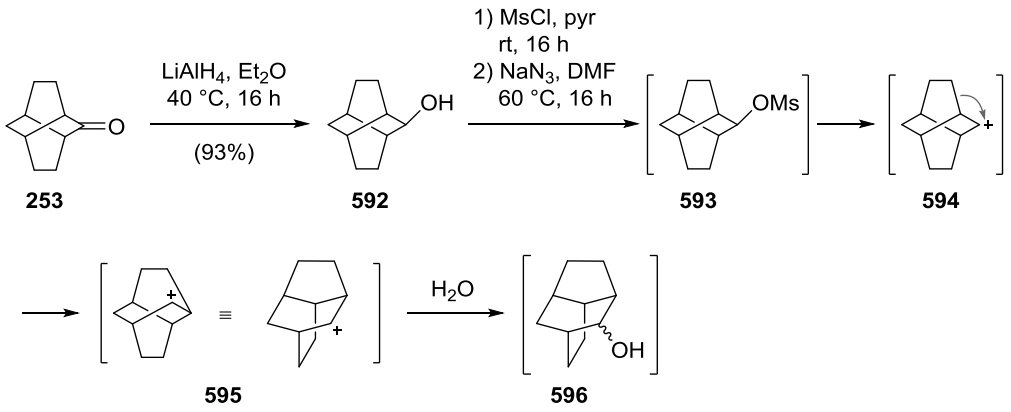
As a consequence, twistenone **470** was submitted to Birch conditions to effect the reduction to twistenol **587** (Scheme 139). Indeed, monitoring of the reaction showed the disappearance of the

starting material but analysis of the product by NMR spectroscopy led to the assignment of structure **591**. This species presumably is formed by the one-electron reduction of ketone **470** to ketyl radical **588**, which subsequently cyclizes in a 3-*exo-trig* process to cyclopropylcarbinyl radical **589**. The cyclopropane opens to homoallyl radical **590**, which then gets reduced and protonated to result in allylic alcohol **591**. This kind of reactivity has not yet been reported for *β*,*γ*-unsaturated ketones to the best of our knowledge. However, cyclizations of ketyl radicals generated by Birch conditions resulting in the formation of five-membered rings are known.[249]



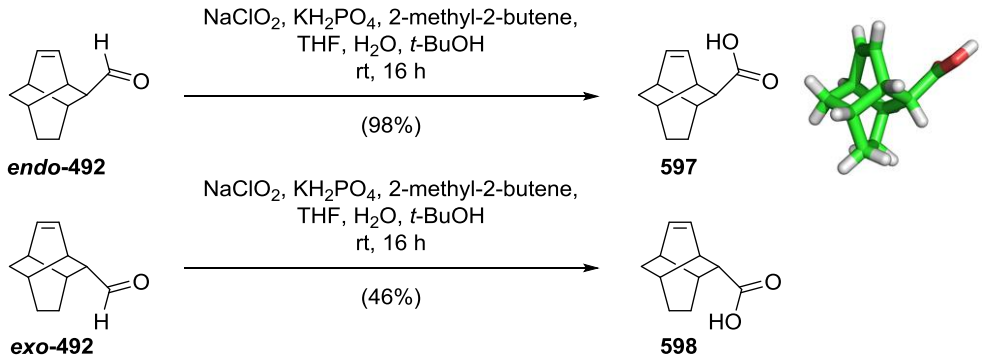
Scheme 139. Presumable mechanism for the formation of allylic alcohol **591**.

In contrast, the reduction of twistanone **253** proceeded smoothly to provide twistanol **592** (Scheme 140).[118] However, first efforts to substitute the alcohol moiety *via* mesylate **593** presumably resulted in the formation of isotwistanol **596** by way of Wagner-Meerwein rearrangement of carbocation **594** to its isomer **595**. Studies to isolate intermediate mesylate **593** and characterize isotwistanol **596** cleanly are currently underway.



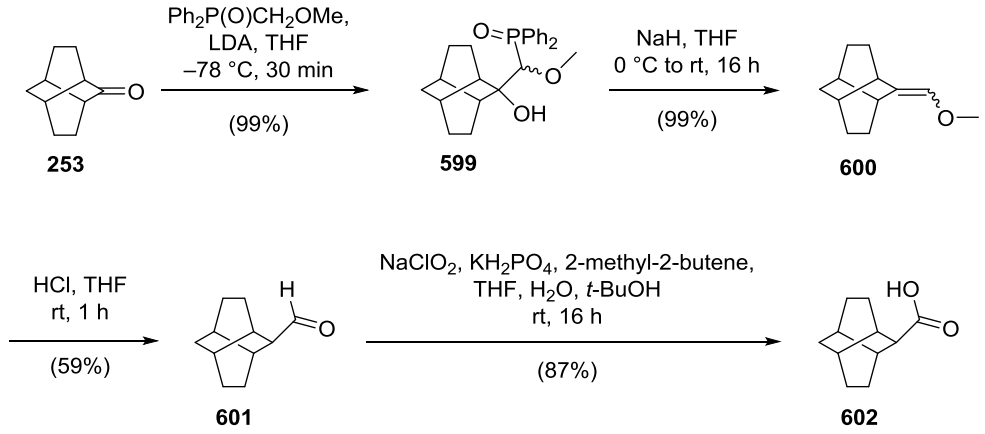
Scheme 140. Presumable formation of isotwistanol **596** from twistanol **592** in nucleophilic substitution attempt.

Next, it was tried to access the desired amines using the Curtius rearrangement. In order to do this, carboxylic acids **597** and **598** were synthesized from their corresponding aldehydes (see Chapter 3.3) using the Pinnick procedure (Scheme 141).[250]



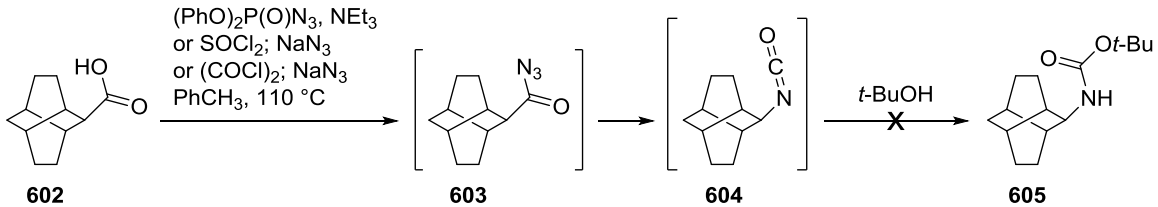
Scheme 141. Synthesis of carboxylic acids **597** and **598**.

For the synthesis of carboxylic acid **602**, twistanone **253** was homologated in an analogous sequence as was carried out for the synthesis of aldehyde **492** (Scheme 111). Thus, twistanone **253** was converted to phosphine oxide **599**, which was subsequently eliminated to enol ether **600** (Scheme 142). Hydrolysis of the enol ether function afforded aldehyde **601** which was then converted in a Pinnick oxidation to saturated carboxylic acid **602**.



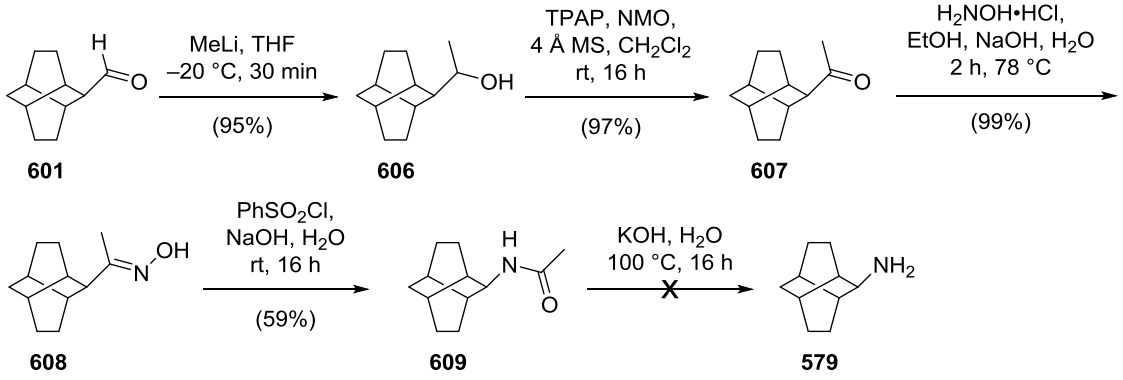
Scheme 142. Synthesis of carboxylic acid **602**.

Subsequently, carboxylic acids **597**, **598** and **602** were submitted to several conditions reported to enable the Curtius reaction. These included the use of diphenylphosphoryl azide to perform the Curtius reaction in one step as well as stepwise efforts *via* intermediate carbonyl azide **603** and isocyanate **604** (Scheme 143).[251],[252] However, it was not possible to isolate the desired carbamate **605** although full conversion of starting material was observed.



Scheme 143. Attempts to perform the Curtius rearrangement on the synthesized carboxylic acids.

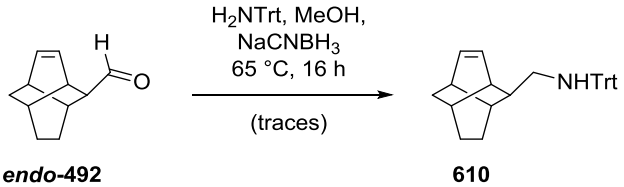
Next, the Beckmann rearrangement was investigated for the installation of the desired amine functionality.[253] Therefore, aldehyde **601** was converted to alcohol **606**, which was subsequently oxidized to ketone **607** (Scheme 144). Transformation of ketone **607** with hydroxylamine provided oxime **608**. The ensuing Beckmann rearrangement afforded amide **609** in moderate yield but enough quantity for the final step. However, the hydrolysis of the amide functionality was not possible using standard basic conditions. Other attempts to cleave the amide moiety and work to synthesize the unsaturated derivatives **580** and **581** using the same procedure with aldehydes ***endo*-492** and ***exo*-492** is currently under progress.



Scheme 144. Synthesis of twistanamine **579** *via* Beckmann rearrangement of oxime **608**.

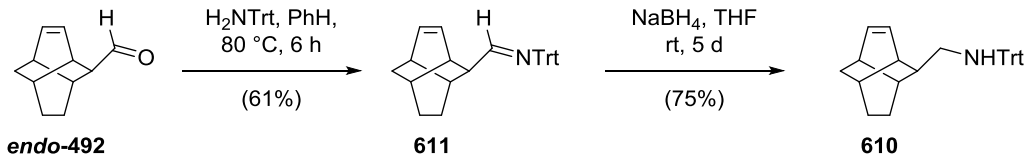
4.2.2 Twistylmethanamines

For the synthesis of twistylmethanamines **582**, **583** and **584**, a protocol for the direct amination of aldehydes using an ammonia equivalent was applied.[248] Thus, aldehyde ***endo*-492** was reacted with tritylamine and sodium cyanoborohydride (Scheme 145). However, only traces of the desired tritylamine **610** were found in the reaction mixture with the major part of the starting material decomposing. The same observation was made if molecular sieves were added to the reaction mixture, sodium acetoxyborohydride was used as the hydride source or if the aldehyde was heated first with the amine and the hydride source was added later.



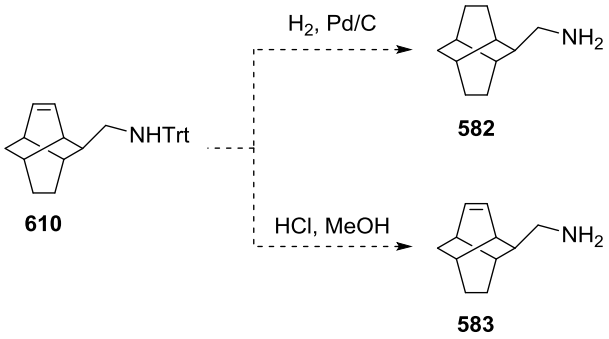
Scheme 145. Attempt to synthesize tritylamine **610** by direct amination of ***endo*-492**.

As a consequence, it was decided to perform the amination in two stages with the intermediate isolation of imine **611**. Boiling tritylamine and aldehyde ***endo*-492** in benzene over 3 Å molecular sieves proceeded smoothly to provide imine **611** (Scheme 146). In contrast, the reduction of imine **611** with sodium borohydride required very long reaction times and did not go to completion. These observations explain the hesitance of the aldehyde to undergo direct amination. Presumably, the imine species forms during this reaction but its high steric demand prevents the reduction.



Scheme 146. Stepwise synthesis of tritylamine **610**.

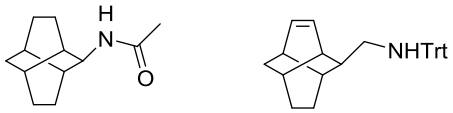
Finally, differentiating deprotection of tritylamine **610** by hydrogenolysis or hydrolysis will give access to twistylmethanamines **582** and twistylmethanamine **583**, respectively.[254]



Scheme 147. Envisioned differentiating deprotection of tritylamine **610** to the desired twistylmethanamines **582** and **583**.

4.3 Conclusion and Future Directions

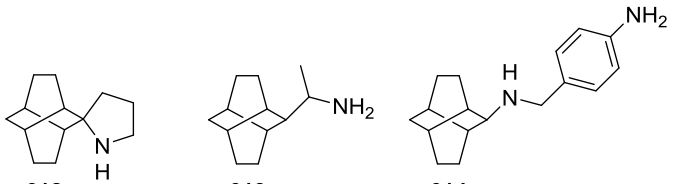
Several novel amines, containing the twistane or homotwistane cage, were designed as potential antiviral agents. Building on the work in Chapter 3, considerable progress was made toward the synthesis of these amines resulting in protected amines **609** and **610** (Figure 30). Additionally, the now established synthesis is applicable to further unsaturated twistane derivatives.



609 **610**

Figure 30. Synthesized protected amines **609** and **610**.

In the future, the synthesis of twistenamines **580** and **581**, as well as **584** has to be completed. Judging from the results of the following biological studies, further structural modifications of the twistanamines can be performed. For example, spiro twistanamines such as **612**, methylated derivatives such as **613** or further functionalized structures like **614** might be interesting for activity against resistant virus strains (Figure 31). Furthermore the effect of enantiopure twistanamines still has to be evaluated. In this regard, it would be most practical to perform an optical resolution of the synthesized twistanamines for example *via* a tartrate salt.

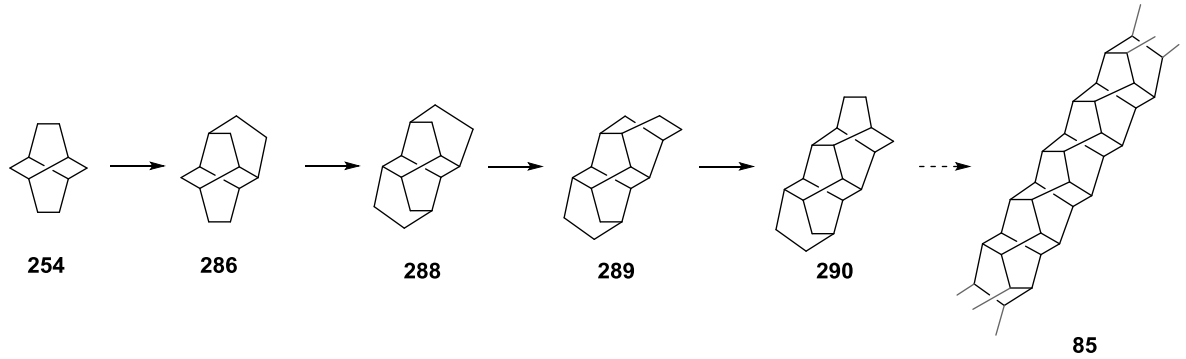


612 **613** **614**

Figure 31. Further amines bearing the twistane cage which might be promising as antiviral agents.

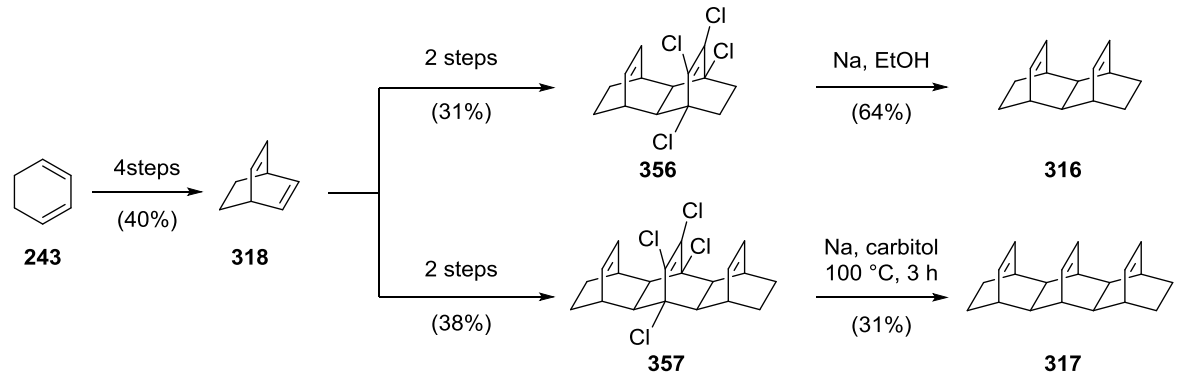
5 Summary

In this PhD thesis, a structurally novel polymer, polytwistane (**85**), was proposed which is conceptually developed by continuous linear extension of twistane (**254**) with ethano units (Scheme 148). The resulting polymer exclusively consists of cyclohexane rings in the D_2-symmetric twist-boat conformation. Thus, polytwistane (**85**) is C_2-symmetric and displays helical chirality. Additionally, the polymer is built up from methine C(sp^3)─H units which are all chemically equivalent. Using computational chemistry it was shown that a polymerization of acetylene to polytwistane (**85**) is highly exothermic.



Scheme 148. Development of polytwistane (**85**) from twistane (**254**) by linear addition of ethano units.

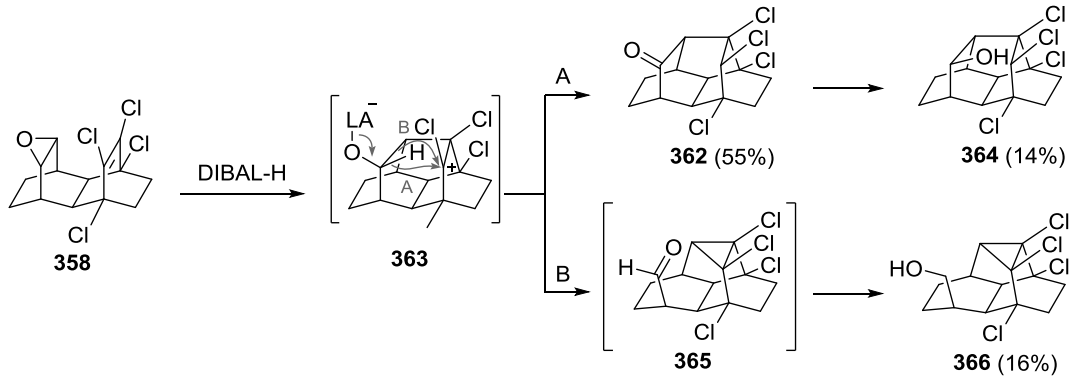
First experimental work was dedicated to the synthesis and characterization of defined oligotwistanes, in order to obtain spectral information which could help to identify polytwistane (**85**) in complex reaction mixtures (Chapter 2). The desired oligotwistane structures were planned to be accessed in electrophilic additions to laticyclic homoconjugated oligoenes such as diene **316** and **317** (Scheme 149). For the synthesis of the respective precursors an improved procedure was developed giving rapid and reliable access to dihydrobarrelene (**318**) and thus allowing the synthesis of dienes **356** and **316** as well as trienes **357** and **317**.



Scheme 149. Improved synthesis of dihydrobarrelene **318** and access to laticyclic conjugated precursors.

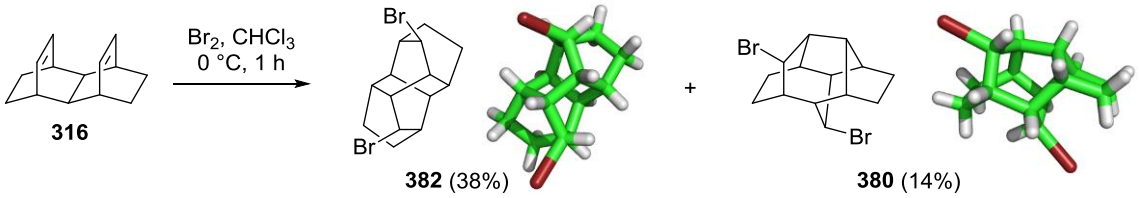
Subsequently the conjugate electrophilic addition was investigated on the diene system. Attempts to effect this transformation *via* epoxidation and ensuing epoxide opening resulted in the formation of

novel carbon scaffolds as present in secondary alcohol **364** or primary alcohol **366** but did not provide the desired C_2-tritwistane framework (Scheme 150).



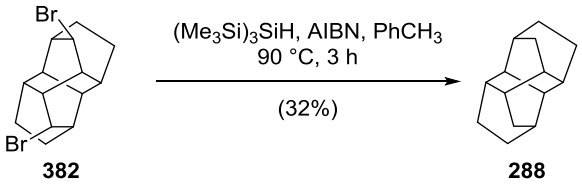
Scheme 150. Conjugate opening of epoxide **358**.

Fortunately, carrying out the transformation using bromine as the electrophilic reagent afforded dibromotritwistane **382** along with structurally interesting dibromide **380** which presumably arises from a double Wagner-Meerwein rearrangement (Scheme 151). Both compounds were characterized by single crystal X-ray diffraction, unambiguously verifying the structure of the reaction products.



Scheme 151. Bromination of diene **316** and X-ray structures of the resulting products.

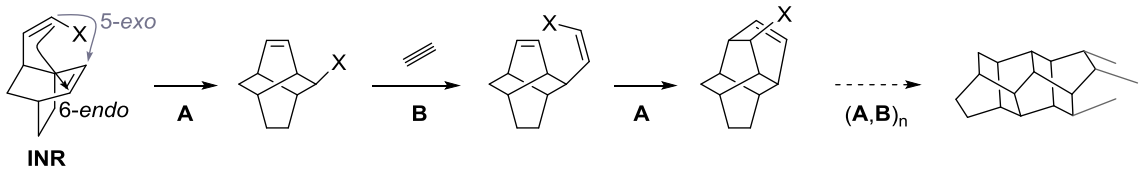
Debromination of dibromotritwistane **382** then was carried out successfully using radical conditions to afford the desired C_2-tritwistane (**288**).



Scheme 152. Debromination of dibromotwistane **382** to afford C_2-tritwistane (**288**).

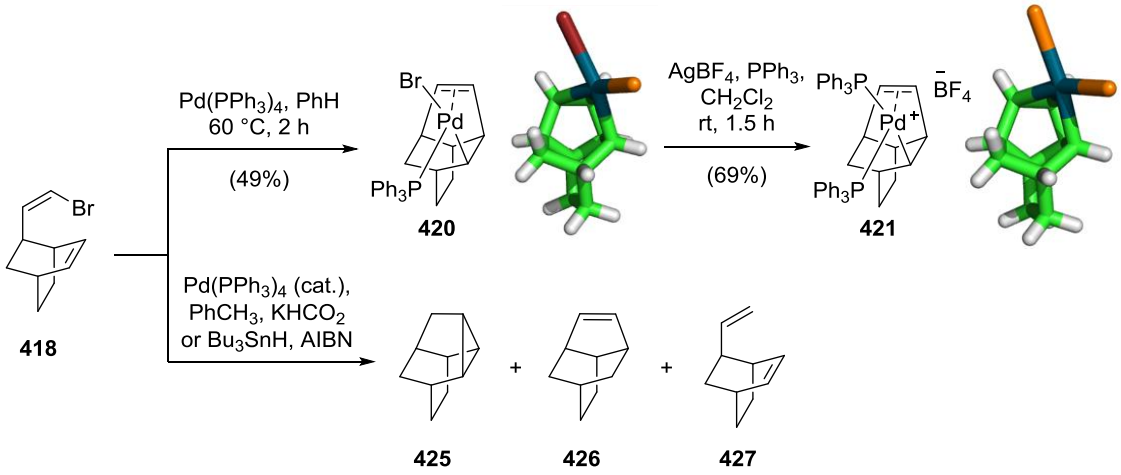
Similar studies toward C_2-hexatwistane (**291**) using trienes **357** or **317** did not result in the formation of the desired product but only led to complex mixtures. An obvious reason might be the multitude of possible rearrangement pathways in the extended laticyclic conjugated system. While the possibility exists that the C_2-hexatwistane cage is formed under these conditions, the observations indicate that this synthetic method is not suitable for the synthesis of higher oligotwistanes or polytwistane.

For the synthesis of polytwistane (**85**) several synthetic strategies were devised (Chapter 3). The initiator-biased polymerization of acetylene was identified as the most promising possibility (Scheme 153). This process was envisioned to commence with an initiator compound **INR**, which was planned to exhibit the structural bias toward the desired helical structure, and to proceed with alternating intramolecular cyclizations (**A**) and intermolecular additions to acetylene (**B**). It was intended to exploit transition metal catalysis as well as radical conditions for the realization of this process.



Scheme 153. Proposed acetylene polymerization for the synthesis of polytwistane (**85**).

To investigate the regioselectivity (5-*exo-trig* vs. 6-*endo-trig*) of the crucial intramolecular cyclization step of the envisioned polymerization, the simple bicyclic initiator compound **418** was synthesized and submitted to transition metal-catalytic as well as radical conditions to enable the cyclization (Scheme 154). However, the only products found were the result of a 5-*exo-trig* cyclization. This was unambiguously confirmed by X-ray structures of products obtained from reactions with stoichiometric amounts of palladium.



Scheme 154. Investigation of the crucial cyclization step on initiator compound **418**.

As a consequence, modified bicyclic initiator compounds **438**, **439** and **440** were synthesized in order to influence the regioselectivity of the cyclization. However, all ensuing cyclization attempts using these molecules afforded only 5-*exo-trig* cyclization products such as **452** to **455**, but provided the X-ray structure of a rare alkenylpalladium complex **448** (Figure 32). Computational studies on the relative energy of the cyclization products supported the observed regioselectivity and indicated that an extended initiator system might facilitate the desired cyclization mode.

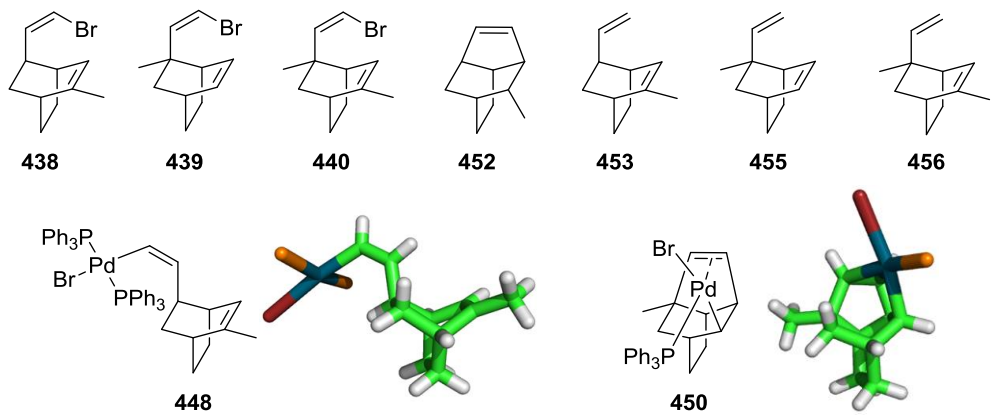
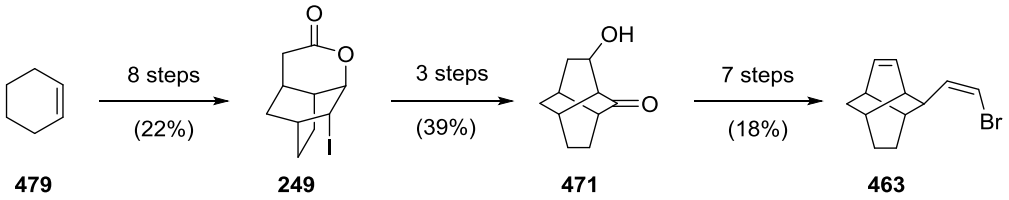


Figure 32. Modified bicyclic initiator compounds and respective products from cyclization attempts.

As a result of the thermodynamic calculations, the cyclization was to be tested on tricyclic initiator compound **463**. For the synthesis of this precursor a reliable and scalable route was developed commencing with iodolactone **249**, which was available in 8 steps from cyclohexene (**479**) on multi-gram scale (Scheme 155). The key steps of the synthesis included the generation of the twistane skeleton by an aldol reaction, the elimination of the alcohol moiety in *β*-hydroxyketone **471** *via* reduction of an enol triflate and installation of the alkenyl bromide handle by homologation and subsequent Stork-Zhao reaction.



Scheme 155. Synthesis of tricyclic precursor **463**.

Investigation of the critical cyclization step on alkenyl bromide **463** was carried out using several transition metal catalytic and radical conditions. During these studies the novel hydrocarbon compound **465** and palladium complex **512** were isolated (Figure 33). Characterization of the latter by single crystal X-ray diffraction unambiguously showed that the undesired 5-*exo*-*trig* cyclization mode was operational. All efforts to change the selectivity of the cyclization proved unsuccessful. Therefore, a polymerization leading to polytwistane (**85**) was not yet realized.

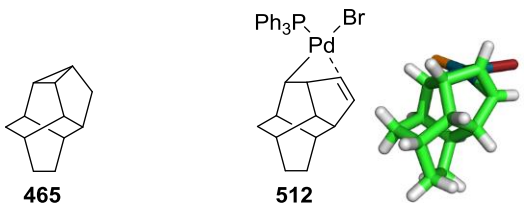
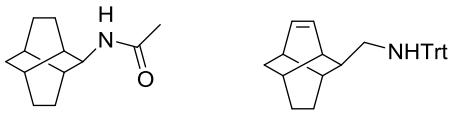


Figure 33. Products from cyclization attempts on tricyclic initiator **463**.

To facilitate the identification of polytwistane (**85**) in possibly complex reaction mixtures, the ^{1}H and ^{13}C NMR chemical shifts of a series of oligotwistanes as large as $C_{46}H_{52}$ were calculated on the B3LYP/6-31+G(d,p)-CPCM-SCRF//B3LYP/6-31G(d) level. For the evaluation of the computational data a linear regression scheme was employed. In order to obtain accurate data, the linear regression was parametrized using a test set of 25 polycyclic compounds, which were available from previous synthetic work or were synthesized for this purpose. Indeed, convergence of the chemical shifts of the methine units was observed for oligotwistanes larger than $C_{32}H_{38}$. In collaboration with the group of Prof. Ochsenfeld (Ludwig Maximilian University of Munich), calculations on a more sophisticated computational level were performed resulting in an expected ^{1}H NMR chemical shift of δ = 1.5 ppm and ^{13}C NMR chemical shift of δ = 33 ppm for ideal polytwistane (**85**).

Based on structural considerations, potential antiviral agents containing the twistane scaffold were designed in order to target influenza A virus mutants which display resistance against adamantane derived drugs (Chapter 4). The synthesis of twistanamines **609** and **610** proceeded from intermediates of the preparation of tricyclic initiator compound **463** (Figure 34). A reliable access to the desired twistanamines using the Beckmann rearrangement and a stepwise amination procedure was developed. Work to complete the synthesis of the target structures as well as to access other derivatives is currently under investigation.



609 **610**

Figure 34. Synthesized protected twistanamines **609** and **610**.

EXPERIMENTAL PART

6 General Experimental Details

All reactions, unless stated otherwise, were carried out under a positive pressure of N_2 in flame-dried glassware. Commercial reagents and solvents were used as purchased with the following exceptions. Tetrahydrofuran (THF) and diethylether (Et_2O) were pre-dried over $CaCl_2$ and distilled over sodium and benzophenone under a nitrogen atmosphere immediately before use. Triethylamine (NEt_3), diisopropylamine (DIPA) and diisopropylethylamine (DIPEA) were distilled over CaH_2 under a nitrogen atmosphere prior to use. *m*-CPBA was recrystallized from CH_2Cl_2 and stored at –25 °C.[255] Claisen lye was prepared by dissolving KOH (35 g) in H_2O (25 mL) and MeOH (150 mL). Degassing of solvents for sensitive reactions was realized using the freeze-pump-thaw method. Dichloromethane (CH_2Cl_2), Et_2O, ethyl acetate (EtOAc), hexanes and *n*-pentane for flash chromatography and workup were obtained from technical grade by distilling *in vacuo* prior to use. "Hexanes" refers to the fraction of petroleum that boils between 40 °C and 60 °C. All reactions were magnetically stirred and monitored by analytical thin-layer chromatography (TLC) using *Merck* silica gel 60 F_{254} glass-backed plates. Spots were visualized under UV light (254 nm) or by application of aqueous stains of basic potassium permanganate, ceric ammonium molybdate, anisaldehyde, dinitrophenylhydrazine or vanillin followed by heating with a heat gun. The statement of drying a combined organic layer includes the removal of the drying agent by filtration and washing of the residue with an appropriate solvent. Flash column chromatography was performed on *Merck* silica gel 60 (0.040–0.063 mm). Column diameter, fraction size and amount of silica gel were chosen according to the parameters given by Still *et al.*.[256] Information given in the experimental part corresponds to the format "(diameter of column x height of gel, eluant A : eluant B = ratio A : ratio B, fraction size, number of collected fractions)". Yields refer to chromatographically and spectroscopically pure material. Solutions were concentrated at 30 °C using a *Heidolph* Laborota 4000 efficient employing a *vacuubrand* PC 3001 pump, if not specified otherwise. Reactions under high pressure were performed in a 200 mL steel autoclave.The generation of high pressures was realized using a pressure generator by Andreas Hofer Hochdrucktechnik GmbH with a polytetrafluoroethene (teflon) inlet at the MPI für Kohlenforschung (Mülheim).

Instrumentation

Nuclear magnetic resonance (NMR) spectra were recorded in $CDCl_3$, DMSO-d_6 or C_6D_6 on a *Varian* VNMRS 300, VNMRS 400, INOVA 400, VNMRS 600 or a *Bruker* AVANCEIIIHD 400 spectrometer. Chemical shifts (δ) were calibrated using the residual undeuterated solvent as an internal reference and are according to the common convention reported in *parts per million* (ppm) downfield relative to tetramethylsilane (TMS). The chemical shifts of the reference solvents were defined concurrent with the data from Nudelman and coworkers[257] for $CDCl_3$: 7.26 ppm (^{1}H NMR) and 77.16 ppm (^{13}C NMR), for DMSO-d_6: 2.50 ppm (^{1}H NMR) and 39.52 ppm (^{13}C NMR) and for C_6D_6: 7.16 ppm (^{1}H NMR) and 128.06 ppm (^{13}C NMR). For the designation of multiplicities the following

abbreviations were used: s (singlet), d (doublet), t (triplet), br (broad) and m (multiplet) or combinations thereof. Protons and carbons were assigned using 2D spectra (HSQC, COSY, NOESY, HMBC) and the assignment is corresponding to the numbering of the given structure. Numbering in the structures for NMR analysis is chosen for clarity and does not necessarily conform to IUPAC recommendations. If unequivocal assignment of signals was not possible, the assigned atoms are marked with "*". "**", "***" and are mutually exchangeable. Coupling constants $^{n}J_{A,B}$ are given between atoms A and B over n bonds and reported in Hz. Diastereotopic protons are named H_A and H_B where they could not be unambiguously assigned. Analysis of all spectra was performed with MestReNova Version 5.2.5. by *Mestrec Laboratories*.

Infrared (IR) spectra were recorded on a *Perkin Elmer* Spectrum BX-59343 instrument with a *Smiths Detection* DuraSampl*IR* II Diamond ATR sensor for detection in the range from 4500 cm^{-1} to 600 cm^{-1}. Samples were prepared as a film for liquid or neat for solid substances. Data in the experimental part are given in units of cm^{-1} and the intensities are given with vw (very weak), w (weak), m (medium), s (strong) and vs (very strong).

High resolution (HRMS) and low resolution (LRMS) mass spectra were recorded on a *Finnigan* MAT 90 and a *Finnigan* MAT 95 instrument. Ionization of the samples was achieved using electrospray ionization (ESI) or electron ionization (EI). In the experimental part only the high resolution mass peak is given and the used mode of ionization is stated.

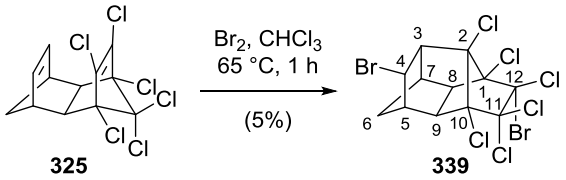
Melting points were measured on a *BÜCHI* B-540 melting point apparatus and are given in uncorrected form.

All single crystal X-ray diffraction experiments were carried out by Dr. Peter Mayer in the analytics department. The CrysAlisPro software (version 1.171.33.41) was applied for the integration, scaling and multi-scan absorption correction of the data.[258] The structures were solved by direct methods with SIR97 and refined by least-squares methods against *F2* with SHELXL-97.[259],[260]

7 Experimental Procedures

7.1 Synthesis of C_2-Tritwistane

4,12-Dibromo-1,2,10,11,11,12-hexachloropentacyclo[6.4.0.0^{2,10}.0^{3,7}.0^{5,9}]dodecane (339)



To a solution of isodrine **325** (9.12 g, 25.0 mmol, 1.00 eq.) in $CHCl_3$ (100 mL) at 0 °C was added a solution of bromine (1.28 mL, 4.00 g, 25.0 mmol, 1.00 eq.) in $CHCl_3$ (25.0 mL). The resulting mixture was allowed to warm to room temperature and was subsequently heated to 65 °C for 1 h. The reaction mixture was allowed to cool to room temperature and was washed with saturated aqueous $Na_2S_2O_3$ (100 mL), saturated aqueous $NaHCO_3$ (100 mL), H_2O (100 mL), dried ($CaCl_2$) and concentrated *in vacuo*. Purification of the resulting brown solid by recrystallization from MeOH : acetone (1 : 1) afforded rearranged dibromide **339** (650 mg, 5%) contaminated with an unseparable impurity as a colorless solid. The obtained crystals were suitable for single crystal X-ray diffraction.

$C_{12}H_{18}Br_2Cl_6$ M_r = 524.72 g·mol^{-1}.

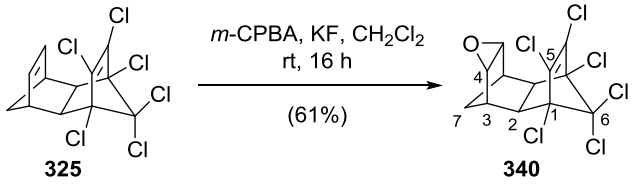
^{1}H NMR (400 MHz, $CDCl_3$): δ = 5.73 (dd, $^3J_{C4\text{-}H,C5\text{-}H}$ = 1.7 Hz, $^4J_{C4\text{-}H,C6\text{-}Hexo}$ = 1.7 Hz, 1H, C4-H), 3.18 – 3.12 (m, 2H, C7-H, C9-H), 3.01 – 2.97 (m, 1H, C3-H), 2.90 (ddd, $^3J_{C8\text{-}H,C9\text{-}H}$ = 7.1 Hz, $^3J_{C8\text{-}H,C7\text{-}H}$ = 2.9 Hz, $^3J_{C8\text{-}H,C3\text{-}H}$ = 1.7 Hz, 1H, C8-H), 2.85 – 2.81 (m, 1H, C5-H), 2.53 (ddd, $^2J_{C6\text{-}Hendo,C6\text{-}Hexo}$ = 11.5 Hz, $^3J_{C6\text{-}Hendo,C7\text{-}H}$ = 2.6 Hz, $^3J_{C6\text{-}Hendo,C5\text{-}H}$ = 1.1 Hz, 1H, C6-H$_{endo}$), 1.54 (ddd, $^2J_{C6\text{-}Hexo,C6\text{-}Hendo}$ = 11.5 Hz, $^3J_{C6\text{-}Hexo,C5\text{-}H}$ = 1.8 Hz, $^4J_{C6\text{-}Hexo,C4\text{-}H}$ = 1.7 Hz, 1H, C6-H$_{exo}$) ppm.

^{13}C NMR (75 MHz, $CDCl_3$): δ = 102.4 (C11), 88.1 (C12), 83.5 (C1*), 81.4 (C10*), 78.8 (C2), 61.3 (C3), 58.7 (C8), 50.6 (C4), 47.6 (C9), 46.1 (C5), 45.7 (C7), 33.7 (C6) ppm.

IR (ATR): $\tilde{\nu}$ = 2989 (vw), 1753 (w), 1732 (vw), 1707 (vw), 1598 (vw), 1456 (vw), 1436 (vw), 1376 (vw), 1339 (vw), 1287 (w), 1280 (m), 1265 (m), 1246 (w), 1225 (w), 1209 (w), 1178 (w), 1126 (w), 1114 (w), 1097 (m), 1084 (w), 1054 (m), 1046 (w), 1026 (m), 1020 (m), 1008 (s), 966 (w), 954 (w), 943 (w), 933 (m), 908 (m), 885 (m), 866 (m), 845 (m), 829 (m), 798 (m), 770 (s), 756 (m), 744 (vs), 718 (s), 710 (s), 698 (s), 684 (m), 668 (m) cm^{-1}.

HRMS (EI): m/z for $C_{12}H_{18}Br_2Cl_6^+$ $[M]^+$: calcd.: 519.7118
found: 519.7104.

4,5-Epoxy-1,8,9,10,11,11-hexachlorotetracyclo[6.2.1.1^{3,6}.0^{2,7}]dodec-9-ene (340)



To a solution of isodrine **325** (5.00 g, 13.7 mmol, 1.00 eq.) in CH_2Cl_2 (15.0 mL) at room temperature was added *m*-CPBA (72.5 wt-%, 6.52 g, 27.4 mmol, 2.00 eq.) and KF (1.59 g, 27.4 mmol, 2.00 eq.). The resulting mixture was stirred at room temperature for 16 h. After this time, activated (120 °C, 0.04 mbar, 1 h) KF (1.59 g, 27.4 mmol, 2.00 eq.) was added and the reaction mixture was stirred for an additional 1 h. The reaction mixture was filtered and the residue was washed with CH_2Cl_2 (50 mL). The combined filtrate was concentrated *in vacuo* to afford epoxide **340** (3.16 g, 61%) as a colorless solid.

$C_{12}H_8Cl_6O$ M_r = 380.91 g·mol^{-1}.

TLC R_f = 0.25 (hexanes : EtOAc = 20 : 1).

mp 216 – 219 °C.

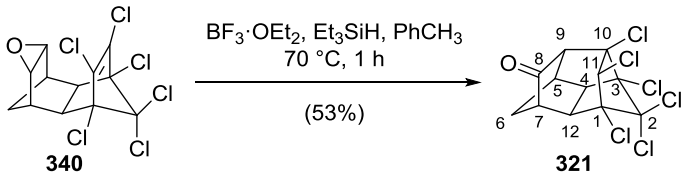
^{1}H NMR (600 MHz, $CDCl_3$): δ = 3.34 – 3.31 (m, 2H, C4-H), 3.24 (dd, $^3J_{C2\text{-}Ha,C2\text{-}Hb}$ = 2.5 Hz, $^3J_{C2\text{-}H,C3\text{-}H}$ = 1.5 Hz, 2H, C2-H), 2.91 – 2.89 (m, 2H, C3-H), 1.80 (dt, $^2J_{C7\text{-}Hanti,C7\text{-}Hsyn}$ = 10.3 Hz, $^3J_{C7\text{-}Hanti,C3\text{-}H}$ = 2.0 Hz, 1H, C7-H$_{anti}$), 0.97 – 0.93 (m, 1H, C7-H$_{syn}$) ppm.

^{13}C NMR (150 MHz, $CDCl_3$): δ = 132.5 (C5), 108.9 (C6), 79.7 (C1), 54.8 (C2), 47.3 (C4), 39.4 (C3), 30.0 (C7) ppm.

IR (ATR): $\tilde{\nu}$ = 3066 (vw), 3058 (vw), 3015 (vw), 2981 (vw), 2960 (vw), 2890 (vw), 1599 (w), 1457 (vw), 1374 (vw), 1300 (vw), 1263 (w), 1234 (w), 1178 (w), 1138 (vw), 1114 (vw), 1072 (w), 1047 (w), 1007 (w), 979 (w), 954 (vw), 944 (w), 905 (w), 886 (m), 847 (vs), 805 (w), 747 (s), 719 (s), 682 (m), 608 (vw), 580 (s), 560 (s) cm^{-1}.

HRMS (EI): m/z for $C_{12}H_8Cl_6O^+$ $[M]^+$: calcd.: 377.8701
found: 377.8696.

1,2,2,3,10,11-Hexachloropentacyclo[5.4.1.0^{3,10}.0^{4,12}.0^{5,9}]dodecan-8-one (321)



To a solution of epoxide **340** (152 mg, 0.400 mmol, 1.00 eq.) in toluene (10.0 mL) at 70 °C was added $BF_3{\cdot}OEt_2$ (0.060 mL, 0.460 mmol, 1.15 eq.) and Et_3SiH (0.070 mL, 0.440 mmol, 1.10 eq.) in toluene (5.00 mL). The resulting mixture was stirred at 70 °C for 1 h, was then allowed to cool to room temperature and quenched with aqueous KH_2PO_4 (1 M, 35 mL). The mixture was extracted with $CHCl_3$ (5 x 50 mL) and the combined organic layer was washed with H_2O (150 mL), dried (Na_2SO_4) and concentrated *in vacuo*. Purification of the residue by flash column chromatography (1 x 26 cm, silica, $CHCl_3$, 8 mL, #4–9) afforded ketone **321** (80 mg, 53%) as a colorless solid. Recrystallization from CH_2Cl_2/hexanes afforded crystals suitable for single crystal X-ray diffraction.

$C_{12}H_8Cl_6O$ M_r = 380.91 g·mol^{-1}.

TLC R_f = 0.66 ($CHCl_3$).

mp 260 °C (dec.).

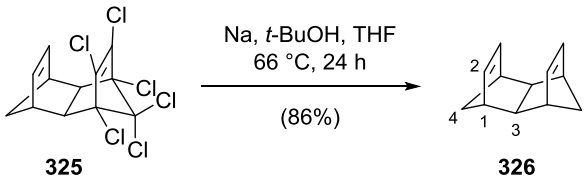
^{1}H NMR (600 MHz, $CDCl_3$): δ = 5.01 (s, 1H, C11-H), 3.39 – 3.32 (m, 2H, C4-H, C12-H), 3.32 – 3.29 (m, 1H, C5-H), 3.12 – 3.09 (m, 1H, C9-H), 2.93 – 2.89 (m, 1H, C7-H), 1.93 – 1.87 (m, 1H, C6-H_A), 1.74 – 1.68 (m, 1H, C6-H_B) ppm.

^{13}C NMR (150 MHz, $CDCl_3$): δ = 205.4 (C8), 97.9 (C2), 86.2 (C3*), 78.8 (C10*), 72.4 (C1), 68.2 (C11), 64.3 (C9), 58.5 (C4), 53.1 (C12), 48.7 (C7), 40.1 (C5), 34.0 (C6) ppm.

IR (ATR): $\tilde{\nu}$ = 2992 (vw), 1750 (vs), 1741 (m), 1458 (vw), 1212 (vw), 1177 (vw), 1116 (w), 1096 (m), 1053 (vw), 1026 (m), 954 (w), 908 (w), 886 (w), 818 (w), 768 (w), 711 (m) cm^{-1}.

HRMS (EI): m/z for $C_{12}H_8Cl_6O^+$ $[M]^+$: calcd.: 377.8706
found: 377.8683.

endo,endo-Tetracyclo[6.2.1.1^{3,6}.0^{2,7}]dodeca-4,9-diene (326)



325 **326**

To a stirred solution of isodrine **325** (16.4 g, 45.0 mmol, 1.00 eq.) and *tert*-butanol (51.0 g, 689 mmol, 15.3 eq.) in THF (200 mL) at room temperature, sodium (20.0 g, 871 mmol, 19.4 eq.) was added in small portions. After complete addition, the mixture was heated to 66 °C for 24 h. After removal of excess sodium the mixture was hydrolyzed at room temperature with H_2O (150 mL), extracted four times with hexanes (300, 200, 100, 50 mL) and the combined extracts were dried ($MgSO_4$). The solvent was removed *in vacuo* and distillation of the residue at 70 °C and 5 mbar gave diene **326** (6.12 g, 86%) as a yellow oil.

$C_{12}H_{14}$ M_r = 158.24 g·mol^{-1}.

TLC R_f = 0.67 (hexanes).

mp 30 – 32 °C.

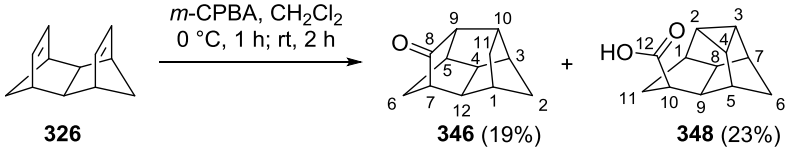
^{1}H NMR (300 MHz, $CDCl_3$): δ = 5.36 – 5.23 (m, 4H, C2-H), 2.76 – 2.73 (m, 2H, C3-H), 2.61 – 2.57 (m, 4H, C1-H), 1.50 – 1.48 (m, 4H, C4-H) ppm.

^{13}C NMR (75 MHz, $CDCl_3$): δ = 131.6 (C2), 55.7 (C4), 44.7 (C1), 43.1 (C3) ppm.

IR (ATR): $\tilde{\nu}$ = 3059 (vw), 2958 (m), 2864 (w), 2361 (vw), 1745 (w), 1634 (vw), 1573 (vw), 1451 (vw), 1375 (vw), 1338 (w), 1272 (vw), 1251 (w), 1232 (vw), 1218 (vw), 1129 (vw), 1092 (vw), 1069 (vw), 995 (vw), 966 (vw), 908 (w), 884 (w), 872 (w), 841 (vw), 803 (w), 782 (vw), 754 (w), 713 (vs), 690 (w), 668 (vw), 646 (vw), 620 (vw) cm^{-1}.

HRMS (EI): m/z for $C_{12}H_{14}^+$ $[M]^+$: calcd.: 158.1090
found: 158.1091.

Epoxidation of *endo,endo*-Tetracyclo[6.2.1.1^{3,6}.0^{2,7}]dodeca-4,9-diene (326)



326 **346** (19%) **348** (23%)

To a solution of diene **326** (1.00 g, 6.32 mmol, 1.00 eq.) in CH_2Cl_2 (100 mL) at 0 °C was added *m*-CPBA (72.5 wt-%, 1.50 g, 6.32 mmol, 1.00 eq.). The reaction mixture was stirred at 0 °C for 1 h and was then allowed to reach room temperature and stirred at this temperature for an additional 2 h. The mixture was diluted with CH_2Cl_2 (400 mL), poured into aqueous NaOH (10 wt-%, 400 mL), and

extracted with CH_2Cl_2 (150, 100 mL). The combined organic layer was successively washed with H_2O (2 x 300 mL) and brine (300 mL), dried ($MgSO_4$), and concentrated *in vacuo*. The residue was purified by flash column chromatography (5 x 20 cm, silica, hexanes : EtOAc = 100 : 1 to 9 : 1, 100 mL) to afford ketone **346** (#15–16, 205 mg, 19%) as a colorless solid and carboxylic acid **348** (#38–73, 271 mg, 23%) as a colorless soild. Recrystallization of carboxylic acid **348** from CH_2Cl_2/hexanes provided crystals suitable for single crystal X-ray diffraction.

*Pentacyclo[5.4.1.0^{3,10}.0^{4,12}.0^{5,9}]dodecan-8-one (**346**)*

$C_{12}H_{14}O$ M_r = 174.24 g·mol^{-1}.

TLC R_f = 0.31 (hexanes : EtOAc = 9 : 1).

mp 164 – 166 °C.

^{1}H NMR (600 MHz, $CDCl_3$): δ = 2.64 – 2.59 (m, 1H, C5-H), 2.56 – 2.52 (m, 3H, C3-H, C4-H, C9-H), 2.47 – 2.38 (m, 2H, C10-H, C12-H), 2.32 – 2.27 (m, 1H, C7-H), 2.25 – 2.20 (m, 1H, C1-H), 1.85 – 1.82 (m, 1H, C6-H$_{exo}$), 1.79 – 1.75 (m, 2H, C11-H$_{endo}$, C2-H$_{exo}$), 1.60 – 1.56 (m, 1H, C6-H$_{endo}$), 1.44 – 1.39 (m, 1H, C2-H$_{endo}$), 1.35 – 1.27 (m, 1H, C11-H$_{exo}$) ppm.

^{13}C NMR (150 MHz, $CDCl_3$): δ = 217.5 (C8), 54.1 (C4), 53.4 (C9), 50.7 (C7), 46.8 (C3), 44.5 (C12), 43.3 (C2), 41.3 (C5), 38.9 (C10), 37.8 (C1), 37.5 (C6), 34.9 (C11) ppm.

IR (ATR): $\tilde{\nu}$ = 3464 (vw), 2951 (m), 2875 (w), 1737 (vs), 1541 (vw), 1488 (vw), 1457 (vw), 1365 (vw), 1327 (vw), 1308 (vw), 1293 (vw), 1281 (vw), 1271 (vw), 1234 (w), 1201 (vw), 1177 (vw), 1169 (w), 1139 (w), 1121 (vw), 1091 (vw), 1068 (vw), 1036 (w), 1006 (vw), 997 (vw), 974 (vw), 954 (vw), 922 (vw), 912 (w), 875 (vw), 862 (vw), 847 (w), 818 (vw), 783 (w), 772 (w), 762 (vw), 742 (vw), 709 (vw), 676 (vw) cm^{-1}.

HRMS (EI): m/z for $C_{12}H_{14}O^+$ $[M]^+$: calcd.: 174.1039
found: 174.1032.

*Pentacyclo[6.3.0.0^{2,4}.0^{3,7}.0^{5,9}]undecane-10-carboxylic acid (**348**)*

$C_{12}H_{14}O_2$ M_r = 190.24 g·mol^{-1}.

TLC R_f = 0.44 (hexanes : EtOAc = 9 : 1).

mp 125 – 127 °C.

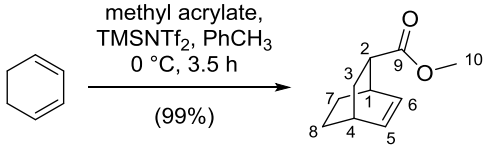
^{1}H NMR (300 MHz, $CDCl_3$): δ = 11.38 (br s, 1H, OH), 2.98 (ddd, $^3J_{C1\text{-}H,C9\text{-}Ha}$ = 11.4 Hz, $^3J_{C1\text{-}H,C2\text{-}H}$ = 8.6 Hz, $^3J_{C1\text{-}H,C9\text{-}Hb}$ = 2.9 Hz, 1H, C10-H), 2.69 – 2.62 (m, 1H, C7-H), 2.62 – 2.56 (m, 1H, C1-H), 2.56 – 2.50 (m, 1H, C11-H$_{syn}$), 2.50 – 2.45 (m, 1H, C5-H), 2.45 – 2.38 (m, 1H, C8-H), 2.37 – 2.29 (m, 1H, C9-H), 2.07 – 2.01 (m, 1H, C6-H$_B$), 2.00 – 1.93 (m, 1H, C11-H$_A$), 1.93 – 1.88 (m, 1H, C3-H), 1.72 – 1.66 (m, 1H, C6-H$_A$), 1.59 – 1.51 (m, 1H, C2-H), 1.13 – 1.03 (m, 1H, C4-H) ppm.

^{13}C NMR (75 MHz, $CDCl_3$): δ = 181.6 (C12), 52.9 (C6), 51.6 (C8), 50.5 (C9), 47.3 (C1), 45.6 (C7), 43.1 (C10), 41.3 (C5), 36.7 (C2), 34.0 (C3), 32.8 (C11), 21.3 (C4) ppm.

IR (ATR): $\tilde{\nu}$ = 3040 (w), 3024 (w), 2959 (m), 2904 (m), 2878 (w), 1695 (vs), 1447 (vw), 1414 (m), 1345 (w), 1332 (m), 1304 (m), 1285 (m), 1250 (m), 1224 (vs), 1200 (m), 1156 (w), 1096 (w), 1073 (w), 1059 (w), 1043 (w), 1018 (w), 992 (w), 972 (m), 914 (m), 887 (m), 818 (w), 788 (s), 762 (m), 738 (w), 707 (m), 692 (m), 641 (m), 612 (w) cm^{-1}.

HRMS (EI): m/z for $C_{12}H_{14}O_2^+$ $[M]^+$: calcd.: 190.0988
found: 190.0988.

Methylbicyclo[2.2.2]oct-5-ene-2-*endo*-carboxylate (352)



243 **352**

Within a glovebox bis(trifluoromethane)sulfonamide (26.4 g, 93.8 mmol, 0.150 eq.) was weighed into a one necked flask. Allyltrimethylsilane (29.8 mL, 21.4 g, 188 mmol, 0.300 eq.) was added outside of the glovebox at 0 °C with stirring and stirring was continued at room temperature until the end of gas evolution. The reaction mixture was concentrated for 1 h under high vacuum. The residue was dissolved in toluene (1.25 L) and methyl acrylate (56.3 mL, 53.8 g, 0.625 mol, 1.00 eq.) and cyclohexadiene **243** (89.4 mL, 75.1 g, 0.938 mol, 1.50 eq.) were added successively at 0 °C to the solution. The reaction mixture was stirred at 0 °C for 3.5 h, after which time 880 mL of a saturated aqueous $NaHCO_3$ solution were added to the violet reaction mixture. The resulting mixture was stirred at room temperature for 1 h during which time it turned yellow. The organic layer was separated and the aqueous layer was extracted with CH_2Cl_2 (3 x 600 mL). The combined organic layer was dried ($MgSO_4$) and concentrated *in vacuo*. Purification of the residue by flash column chromatography (20 x 40 cm, silica, hexanes : EtOAc = 9 : 1, 100 mL, #17–70) afforded bicycloester **352** as a colorless oil (104 g, 99%).

$C_{10}H_{14}O_2$ M_r = 166.22 g·mol^{-1}.

TLC R_f = 0.44 (hexanes : EtOAc = 9 : 1).

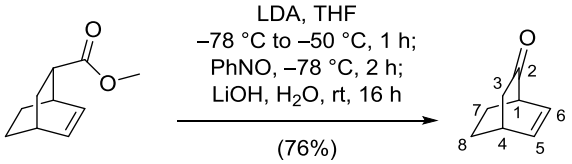
^{1}H NMR (300 MHz, $CDCl_3$): δ = 6.35 – 6.27 (m, 1H, C5-H), 6.18 – 6.11 (m, 1H, C6-H), 3.63 – 3.62 (s, 3H, C10-H), 2.96 – 2.88 (m, 1H, C1-H), 2.67 – 2.56 (m, 2H, C2-H, C4-H), 1.79 – 1.64 (m, 2H, C3-H_{endo}, C3-H_{exo}), 1.60 – 1.45 (m, 2H, C7-H_{syn}, C8-H_{syn}), 1.33 – 1.19 (m, 2H, C7-H_{anti}, C8-H_{anti}) ppm.

^{13}C NMR (75 MHz, $CDCl_3$): δ = 176.1 (C9), 135.3 (C5), 131.5 (C6), 51.8 (C10), 42.8 (C2), 32.6 (C1), 30.0 (C3), 29.5 (C4), 25.5 (C7), 24.5 (C8) ppm.

IR (ATR): $\tilde{\nu}$ = 3045 (vw), 2943 (m), 2866 (w), 2359 (vw), 1733 (vs), 1615 (vw), 1453 (w), 1434 (m), 1374 (w), 1351 (w), 1320 (w), 1288 (vw), 1235 (w), 1195 (s), 1171 (vs), 1120 (vw), 1081 (w), 1054 (m), 1031 (w), 979 (vw), 945 (vw), 889 (w), 850 (vw), 833 (vw), 816 (vw), 801 (vw), 763 (vw), 698 (s) cm^{-1}.

HRMS (EI): m/z for $C_{10}H_{14}O_2^+$ $[M]^+$: calcd.: 166.0994
found: 166.0982.

Bicyclo[2.2.2]oct-5-en-2-one (353)



352 **353**

To a solution of diisopropylamine (1.70 mL, 12.0 mmol, 1.20 eq.) in THF (28 mL) was added at −78 °C a solution of *n*-butyllithium in hexanes (2.6 M, 4.23 mL, 11.0 mmol, 1.10 eq.). The resulting mixture was stirred at −78 °C for 1 h before a solution of ester **352** (1.66 g, 10.0 mmol, 1.00 eq.) in THF (7.00 mL) was added. During the addition, the color of the reaction mixture turned yellow. The mixture was stirred for an additional 60 min and the reaction mixture was allowed to warm to −50 °C. The mixture was re-cooled to −78 °C and a solution of nitrosobenzene (1.12 g, 10.5 mmol, 1.05 eq.) in THF (6.00 mL) was added. The resulting mixture was stirred for 2 h at −78 °C and was then quenched with H_2O (11 mL) and allowed to warm to room temperature. The solvent was removed *in vacuo* and the orange residue was taken up in 1,4-dioxane (35 mL) and treated with a solution of LiOH in H_2O (2.00 M, 25.0 mL, 50 mmol, 5.00 eq.). The resulting solution was stirred at room temperature for 16 h and was then extracted with EtOAc (5 x 70 mL). The combined organic layer was washed with brine (2 x 50 mL), dried (Na_2SO_4) and concentrated *in vacuo*. The residue was dissolved in CH_2Cl_2 (70 mL) and 1 M HCl was added (70 mL). The resulting mixture was stirred at room temperature for 30 min. The organic layer was separated, washed with brine (35 mL), dried (Na_2SO_4) and concentrated *in vacuo*. Purification of the residue by flash column chromatography (4 x 15 cm, *n*-pentane : Et_2O = 95 : 5, 20 mL, #34–62) afforded ketone **353** (0.93 g, 76%) as a colorless solid.

$C_8H_{10}O$ M_r = 122.16 g·mol^{-1}.

TLC R_f = 0.21 (hexanes : EtOAc = 9 : 1).

mp 80 – 82 °C.

^{1}H NMR (300 MHz, $CDCl_3$): δ = 6.47 (ddd, $^3J_{C5\text{-}H,C4\text{-}H}$ = 7.9 Hz, $^3J_{C5\text{-}H,C6\text{-}H}$ = 6.5 Hz, $^4J_{C5\text{-}H,C1\text{-}H}$ = 1.2 Hz, 1H, C5-H), 6.19 (ddd, $^3J_{C6\text{-}H,C1\text{-}H}$ = 8.1 Hz, $^3J_{C6\text{-}H,C5\text{-}H}$ = 6.5 Hz, $^4J_{C6\text{-}H,C4\text{-}H}$ = 1.7 Hz, C6-H), 3.16 – 3.07 (m, 1H, C1-H), 3.04 – 2.93 (m, 1H, C4-H), 2.05 – 2.00 (m,

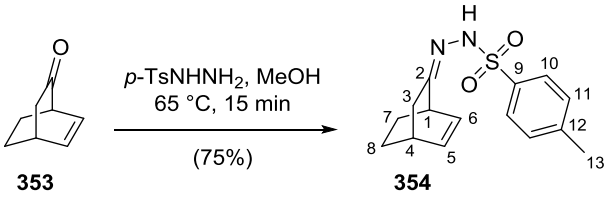
2H, C3-H), 1.90 – 1.79 (m, 1H, C7-H_{exo}), 1.74 – 1.65 (m, 1H, C8-H_{exo}), 1.64 – 1.50 (m, 2H, C7-H_{endo}, C8-H_{endo}) ppm.

^{13}C NMR (75 MHz, $CDCl_3$): δ = 213.3 (C2), 137.2 (C5), 128.6 (C6), 48.7 (C1), 40.6 (C3), 32.5 (C4), 24.4 (C8), 22.6 (C7) ppm.

IR (ATR): $\tilde{\nu}$ = 3053 (vw), 2947 (w), 2911 (vw), 2872 (vw), 1725 (vs), 1448 (vw), 1406 (vw), 1362 (vw), 1268 (vw), 1210 (vw), 1164 (vw), 1086 (w), 1063 (vw), 946 (vw), 904 (vw), 858 (vw), 821 (vw), 745 (vw), 701 (m) cm^{-1}.

HRMS (EI): m/z for $C_8H_{10}O^+$ $[M]^+$: calcd.: 122.0726
found: 122.0728.

Bicyclo[2.2.2]oct-5-en-2-one tosylhydrazone (354)



353 **354**

To a solution of ketone **353** (1.65 g, 13.5 mmol, 1.00 eq.) in MeOH (162 mL) was added *p*-tosylhydrazide (4.27 g, 22.9 mmol, 1.70 eq.). The resulting mixture was heated to 65 °C to dissolve all reagents. The resulting solution was allowed to cool to room temperature was left to stand to allow crystallization. Crystallization was completed by cooling to 0 °C. The precipitate was filtered and washed with cold MeOH and Et_2O to afford hydrazone **354** (2.95 g, 75%) as colorless crystals, which were suitable for single crystal X-ray diffraction.

$C_{15}H_{18}N_2O_2S$ M_r = 290.38 g·mol^{-1}.

TLC R_f = 0.43 (hexanes : EtOAc = 3 : 1).

mp 215 °C (dec.).

^{1}H NMR (400 MHz, DMSO-d_6): δ = 9.81 (s, 1H, N-H), 7.71 (d, $^3J_{C10\text{-}H,C11\text{-}H}$ = 8.1 Hz, 2H, C10-H), 7.38 (d, $^3J_{C11\text{-}H,C10\text{-}H}$ = 8.1 Hz, 2H, C11-H), 6.40 – 6.28 (m, 1H, C5-H), 6.25 – 6.16 (m, 1H, C6-H), 3.05 – 3.00 (m, 1H, C1-H), 2.87 – 2.80 (m, 1H, C4-H), 2.37 (s, 3H, C13-H), 2.16 – 1.96 (m, 2H, C3-H), 1.56 – 1.43 (m, 2H, C7-H_A, C8-H_A), 1.37 – 1.19 (m, 2H, C7-H_B, C8-H_B) ppm.

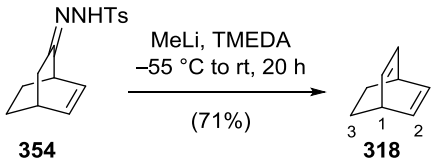
^{13}C NMR (100 MHz, DMSO-d_6): δ = 164.5 (C2), 143.0 (C12), 136.5 (C9), 136.0 (C5), 130.8 (C6), 129.4 (C11), 127.4 (C10), 39.3 (C1), 32.6 (C3), 30.4 (C4), 24.0 (C7*), 23.9 (C8*), 21.0 (C13) ppm.

IR (ATR): $\tilde{\nu}$ = 3212 (m), 3054 (vw), 2948 (w), 2867 (vw), 1740 (vw), 1650 (w), 1596 (w), 1491 (vw), 1445 (vw), 1426 (vw), 1401 (m), 1331 (s), 1292 (m), 1256 (w), 1222

(vw), 1183 (w), 1164 (vs), 1120 (w), 1106 (w), 1091 (m), 1038 (m), 1025 (m), 969 (m), 932 (m), 908 (w), 861 (w), 814 (s), 771 (s), 702 (s) cm^{-1}.

HRMS (ESI+): m/z for $C_{15}H_{19}O_2N_2S^+$ $[M+H]^+$: calcd.: 291.1162
found: 291.1159.

Bicyclo[2.2.2]octa-2,5-diene – Dihydrobarrelene (318)



354 **318**

To a solution of tosylhydrazone **354** (1.78 g, 6.12 mmol, 1.00 eq.) in TMEDA (12.2 mL, 81.1 mmol, 13.3 eq.) at –55 °C was added a solution of methyllithium in Et_2O (1.60 m, 16.8 mL, 26.9 mmol, 4.40 eq.). The resulting yellow mixture was allowed to warm to room temperature and stirred at this temperature for 20 h. The resulting red reaction mixture was cooled to –30 °C, quenched by addition of H_2O (0.75 mL) and subsequently allowed to warm to room temperature. The mixture was diluted with H_2O (50 mL) and extracted with *n*-pentane (5 x 100 mL). The combined organic layer was washed with HCl (2 M, 3 x 150 mL), NaOH (10 wt-%, 2 x 150 mL) and dried (Na_2SO_4). The solvent was removed by careful distillation from a water bath to afford a concentrated solution of dihydrobarrelene (**318**) (~450 mg, 71%) in *n*-pentane. This solution was used for the next step without further purification, due to the volatility of the product. An analytically pure sample of the diene in form of a colorless waxy solid was obtained by sublimation (35 °C, 100 mbar) of a part of the product.

C_8H_{10} M_r = 106.17 $g \cdot mol^{-1}$.

TLC R_f = 0.75 (hexanes).

mp 50 – 53 °C.

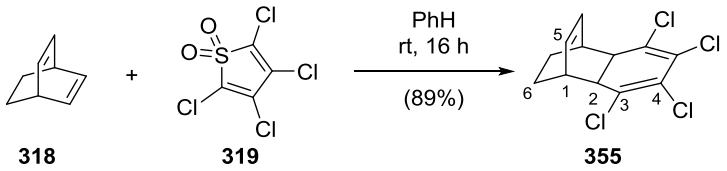
^{1}H NMR (300 MHz, $CDCl_3$): δ = 6.34 – 6.28 (m, 4H, C2-H), 3.67 – 3.57 (m, 2H, C1-H), 1.27 – 1.26 (m, 4H, C3-H) ppm.

^{13}C NMR (75 MHz, $CDCl_3$): δ = 134.5 (C2), 37.1 (C1), 24.9 (C3) ppm.

IR (ATR): $\tilde{\nu}$ = 3054 (w), 2953 (m), 2907 (vw), 2868 (w), 2361 (vw), 2341 (vw), 1634 (vw), 1589 (w), 1460 (vw), 1446 (vw), 1358 (m), 1278 (w), 1224 (w), 1150 (w), 1012 (vw), 944 (w), 908 (m), 823 (m), 809 (w), 700 (vs), 667 (s) cm^{-1}.

HRMS (EI): m/z for $C_8H_{10}^+$ $[M]^+$: calcd.: 106.0777
found: 106.0769.

endo-3,4,5,6-Tetrachlorotricyclo[6.2.2.0^{2,7}]dodeca-3,5,9-triene (355)



318 319 355

To a solution of dihydrobarrelene (**318**) (994 mg, 9.36 mmol, 1.00 eq.) in benzene (40.0 mL) at room temperature was added tetrachlorothiophene dioxide **319** (2.38 g, 9.36 mmol, 1.00 eq.) and the resulting mixture was stirred at room temperature for 12 h. The solvent was removed *in vacuo* and the residue was purified by flash column chromatography (5 x 14 cm, hexanes, 100 mL, #5–9) to afford triene **355** (2.47 mg, 89%) as a colorless solid.

$C_{12}H_{10}Cl_4$ M_r = 296.02 g·mol^{-1}.

TLC R_f = 0.55 (hexanes).

mp 100 – 102 °C.

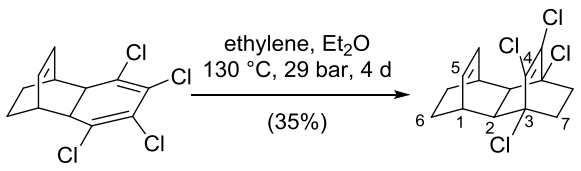
^{1}H NMR (600 MHz, $CDCl_3$): δ = 6.36 – 6.33 (m, 2H, C5-H), 3.25 – 3.21 (m, 2H, C1-H), 3.16 – 3.13 (m, 2H, C2-H), 1.63 – 1.57 (m, 2H, C6-H_{exo}), 1.39 – 1.29 (m, 2H, C6-H_{endo}) ppm.

^{13}C NMR (150 MHz, $CDCl_3$): δ = 134.1 (C5), 132.8 (C4), 123.2 (C3), 48.6 (C2), 33.8 (C1), 24.3 (C6) ppm.

IR (ATR): $\tilde{\nu}$ = 3730 (vw), 3044 (w), 2992 (w), 2961 (w), 2937 (m), 2937 (m), 2910(w), 2886 (w), 2871 (w), 1616 (vs), 1560 (vw), 1462 (vw), 1376 (w), 1339 (w), 1262 (vw), 1227 (vw), 1215 (m), 1184 (w), 1168 (m), 1098 (m), 1034 (w), 1002 (w), 925 (vw), 878 (w), 834 (m), 816 (w) 782 (m), 712 (m), 682 (w), 668 (w) cm^{-1}.

HRMS (EI): m/z for $C_{12}H_{10}Cl_4^+$ $[M]^+$: calcd.: 293.9531
found: 293.9529.

syn-3,4,5,6-Tetrachlorotetracyclo[6.2.2.2^{3,6}.0^{2,7}]tetradeca-4,9-diene (356)



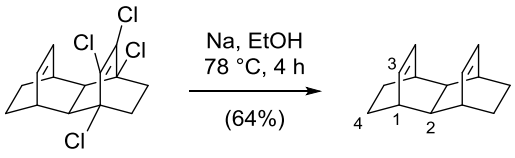
355 356

In the glass liner of an autoclave with 200 mL working space dodecatriene **355** (2.37 g, 8.00 mmol, 1.00 eq.) was dissolved in Et_2O (80.0 mL). The glass liner was furnished with a gas inlet and a gasoutlet and cooled to –110 °C and ethylene (1 L pressure tin) was condensed into the solution. The glass liner was put into a dry-ice cooled autoclave and the autoclave was sealed and heated slowly to 130 °C at which temperature the reaction mixture was stirred for 4 d at a pressure of approximately

29 bar. After cooling to room temperature, excess ethylene was released and the reaction mixture was concentrated *in vacuo*. The residue was purified by flash column chromatography (7.5 x 20 cm, hexanes, 100 mL, #11–20) to afford tetradecadiene **356** (890 mg, 35%) as colorless crystals. Based on recovered starting material (1.455 g, 4.92 mmol, #5–10) a yield of 89% was achieved. Recrystallization of diene **356** from hexanes afforded crystals suitable for single crystal X-ray diffraction.

$C_{14}H_{14}Cl_4$	M_r = 324.08 g·mol^{-1}.
TLC	R_f = 0.47 (hexanes).
mp	87 – 89 °C.
^{1}H NMR	(300 MHz, $CDCl_3$): δ = 6.09 – 5.99 (m, 2H, C5-H), 2.98 – 2.84 (m, 2H, C1-H), 2.38 (br s, 2H, C2-H), 2.20 – 2.10 (m, 2H, C7-H_{exo}), 2.00 – 1.90 (m, 2H, C7-H_{endo}), 1.54 – 1.44 (m, 2H, C6-H_{exo}), 1.29 – 1.18 (m, 2H, C6-H_{endo}) ppm.
^{13}C NMR	(75 MHz, $CDCl_3$): δ = 129.8 (C5), 127.5 (C4), 70.9 (C3), 53.0 (C2), 39.0 (C7), 31.8 (C1), 25.5 (C6) ppm.
IR	(ATR): $\tilde{\nu}$ = 3052 (vw), 2983 (vw), 2965 (vw), 2949 (w), 2937 (vw), 2916 (vw), 2901 (w), 2870 (vw), 2859 (w), 1741 (vw), 1659 (vw), 1594 (w), 1465 (vw), 1442 (vw), 1380 (w), 1364 (vw), 1327 (w), 1308 (vw), 1271 (vw), 1242 (vw), 1219 (vw), 1177 (w), 1114 (vw), 1092 (w), 1070 (vw), 1050 (w), 1026 (vw), 1004 (w), 992 (m), 964 (m), 944 (vw), 906 (w), 862 (w), 846 (m), 819 (w), 760 (s), 719 (vs), 648 (m), 601 (vw), 578 (s) cm^{-1}.
HRMS	(EI): m/z for $C_{14}H_{14}Cl_4^+$ $[M]^+$: calcd.: 324.9844 found: 324.9851.

syn-Tetracyclo[6.2.2.2^{3,6}.0^{2,7}]tetradeca-4,9-diene (316)



356 **316**

A solution of chlorinated diene **356** (502 mg, 1.55 mmol, 1.00 eq.) in EtOH (30.0 mL) was heated to reflux. Sodium (1.78 g, 77.5 mmol, 50.0 eq.) was added in small pieces over a period of 3.5 h and after complete addition the reaction mixture was heated to reflux for an additional 45 min. After cooling to room temperature the reaction slurry was poured on an ice/H_2O mixture (75 g) and was extracted with *n*-pentane (3 x 125 mL). The combined organic layer was washed with H_2O (2 x 125 mL), brine (125 mL), dried (Na_2SO_4) and concentrated *in vacuo*. Purification of the residue by flash column

chromatography (2 x 15 cm, *n*-pentane, 8 mL, #11–13) afforded diene **316** (186 mg, 64%) as a colorless solid.

$C_{14}H_{18}$ M_r = 186.29 g·mol^{-1}.

TLC R_f = 0.79 (hexanes).

mp 55 – 56 °C.

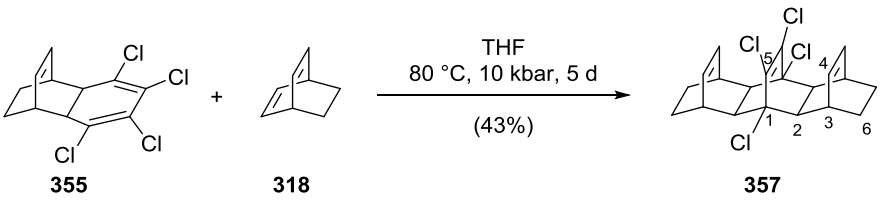
^{1}H NMR (300 MHz, $CDCl_3$): δ = 5.81 – 5.74 (m, 4H, C3-H), 2.34 – 2.24 (m, 4H, C1-H), 1.95 (br s, 2H, C2-H), 1.53 – 1.42 (m, 4H, C4-H_{exo}), 1.14 – 1.03 (m, 4H, C4-H_{endo}) ppm.

^{13}C NMR (75 MHz, $CDCl_3$): δ = 132.1 (C3), 43.8 (C2), 35.3 (C1), 27.3 (C4) ppm.

IR (ATR): $\tilde{\nu}$ = 3043 (w), 3034 (w), 2948 (m), 2931 (s), 2900 (m), 2876 (m), 2861 (m), 2728 (vw), 2666 (vw), 1847 (vw), 1745 (vw), 1683 (vw), 1650 (vw), 1616 (vw), 1462 (vw), 1454 (vw), 1439 (vw), 1396 (vw), 1370 (w), 1326 (vw), 1312 (vw), 1300 (vw), 1278 (vw), 1246 (vw), 1232 (vw), 1222 (vw), 1164 (w), 1116 (vw), 1028 (vw), 986 (vw), 951 (w), 930 (vw), 909 (w), 860 (w), 836 (m), 814 (w), 724 (w), 683 (vs), 649 (m), 572 (w) cm^{-1}.

HRMS (EI): m/z for $C_{14}H_{18}^+$ $[M]^+$: calcd.: 186.1403
found: 186.1402.

all-*syn*-1,8,15,16-Tetrachlorohexacyclo[6.6.2.2^{3,6}.2^{10,13}.0^{2,7}.0^{9,14}]icosa-4,11,15-triene (357)



Dodecatriene **355** (828 mg, 2.80 mmol, 1.00 eq.) was placed in the teflon inlet (10 mL) of an autoclave together with a crystal of 4-*tert*-butylcatechol and was dissolved in THF (6.00 mL). Dihydrobarrelene (**318**) (300 mg, 2.80 mmol, 1.00 eq.) was added. The lid was put on top of the surface of the liquid and the inlet was placed in the autoclave. The reaction mixture was submitted to a pressure of 10 kbar at 80 °C for five days. After cooling to room temperature the reaction mixture was concentrated *in vacuo*. Purification of the residue by flash column chromatography (4 x 15 cm, hexanes, 20 mL, #11–20) afforded chlorinated hexacycloicosatriene **357** (423 mg, 43%) as colorless crystals. Recrystallization from hexanes afforded crystals suitable for single crystal X-ray diffraction.

$C_{20}H_{20}Cl_4$ M_r = 402.19 g·mol^{-1}.

TLC R_f = 0.52 (hexanes).

mp 210°C (dec.).

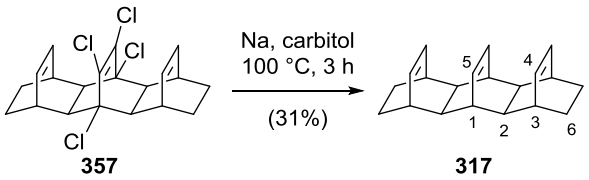
^{1}H NMR (300 MHz, $CDCl_3$): δ = 6.03 – 5.96 (m, 4H, C4-H), 2.99 – 2.89 (m, 4H, C3-H), 2.34 – 2.30 (m, 4H, C2-H), 1.52 – 1.42 (m, 4H, C6-H_{exo}), 1.24 – 1.15 (m, 4H, C6-H_{endo}) ppm.

^{13}C NMR (75 MHz, $CDCl_3$): δ = 130.5 (C4), 124.7 (C5), 75.0 (C1), 54.2 (C3), 31.6 (C2), 25.7 (C6) ppm.

IR (ATR): $\tilde{\nu}$ = 3042 (vw), 2952 (w), 2942 (w), 2906 (vw), 2867 (w), 1648 (vw), 1617 (vw), 1601 (w), 1448 (w), 1386 (vw), 1376 (vw), 1342 (w), 1317 (vw), 1302 (vw), 1280 (w), 1212 (vw), 1187 (w), 1093 (vw), 1077 (vw), 1028 (m), 990 (w), 962 (w), 951 (m), 934 (w), 874 (w), 867 (m), 819 (w), 802 (w), 777 (vw), 756 (s), 719 (vs), 668 (m), 646 (vs), 624 (m), 604 (w), 588 (vw), 580 (vw), 556 (vw) cm^{-1}.

HRMS (EI): m/z for $C_{20}H_{20}Cl_4^+$ [M^+]: calcd.: 403.0314
found: 403.0311.

all-*syn*-Hexacyclo[6.6.2.2^{3,6}.2^{10,13}.0^{2,7}.0^{9,14}]icosa-4,11,15-triene (317)



357 **317**

A solution of chlorinated triene **357** (567 mg, 1.41 mmol, 1.00 eq.) in diethylene glycol monoethyl ether (40.2 mL) was heated to 100 °C. Sodium (1.63 g, 71.0 mmol, 50.4 eq.) was added in small pieces over a period of 2.5 h and after complete addition the reaction mixture was heated to 100 °C for an additional 30 min. After cooling to room temperature the reaction slurry was poured on an ice/H_2O mixture (50 g) and was extracted with *n*-pentane (5 x 35 mL). The combined organic layer was washed with H_2O (2 x 50 mL), brine (25 mL), dried (Na_2SO_4) and concentrated *in vacuo*. Purification of the residue by flash column chromatography (3 x 25 cm, *n*-pentane, 20 mL, #11–14) afforded triene **317** (114 mg, 31%) as a colorless solid. Significant amounts of starting material **357** (175 mg) were recovered.

$C_{20}H_{24}$ M_r = 264.41 g·mol^{-1}.

TLC R_f = 0.75 (hexanes).

mp 141 – 143 °C.

^{1}H NMR (600 MHz, $CDCl_3$): δ = 5.71 – 5.66 (m, 4H, C4-H), 5.28 – 5.24 (m, 2H, C5-H), 2.28 – 2.22 (m, 6H, C1-H, C3-H), 1.98 – 1.94 (m, 4H, C2-H), 1.48 – 1.43 (m, 4H, C6-H_{exo}), 1.07 – 1.01 (m, 4H, C6-H_{endo}) ppm.

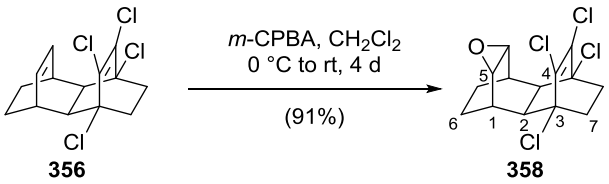
^{13}C NMR (150 MHz, $CDCl_3$): δ = 132.4 (C4), 130.5 (C5), 45.8 (C2), 41.4 (C1), 34.9 (C3), 27.5 (C6) ppm.

IR (ATR): $\tilde{\nu}$ = 3049 (vw), 2923 (vs), 2902 (s), 2867 (s), 1709 (vw), 1613 (vw), 1582 (vw), 1557 (vw), 1460 (w), 1445 (w), 1426 (s), 1376 (m), 1356 (vw), 1344 (vw), 1325 (vw), 1310 (vw), 1295 (w), 1272 (vw), 1228 (vw), 1195 (w), 1170 (w), 1152 (s), 1112

(vw), 1055 (w), 1029 (vw), 1000 (w), 953 (vw), 909 (vw), 889 (vw), 876 (vw), 856 (w), 845 (w), 829 (w), 818 (w), 783 (vw), 733 (m), 708 (vw), 692 (vs), 665 (m) cm^{-1}.

HRMS (EI): m/z for $C_{20}H_{24}^{+}$ $[M]^{+}$: calcd.: 264.1873
found: 264.1875.

9,10-Epoxy-3,4,5,6-tetrachlorotetracyclo[6.2.2.2^{3,6}.0^{2,7}]tetradec-4-ene (358)



356 **358**

To a solution of chlorinated laticyclic diene **356** (250 mg, 0.770 mmol, 1.00 eq.) in CH_2Cl_2 (5 mL) at 0 °C was added *m*-CPBA (266 mg, 1.54 mmol, 2.00 eq.) and KF (89.5 mg, 1.54 mmol, 2.00 eq.). The resulting mixture was stirred at room temperature for 4 d. Then KF (89.5 mg, 1.54 mmol, 2.00 eq.) was added and the reaction mixture was filtered and the residue was washed with CH_2Cl_2. The filtrate was concentrated *in vacuo* and the residue was purified by flash column chromatography (3 x 23 cm, hexanes : EtOAc = 9 : 1, 20 mL, #12–18) to afford epoxide **358** (239 mg, 91%) as a colorless solid. Recrystallization from hexanes afforded crystals suitable for single crystal X-ray diffraction.

$C_{14}H_{14}Cl_4O$ M_r = 340.08 g·mol^{-1}.

TLC R_f = 0.34 (hexanes : EtOAc = 9 : 1).

mp 125 – 127 °C.

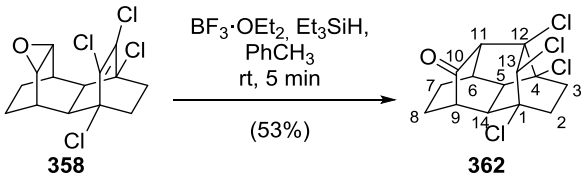
^{1}H NMR (600 MHz, $CDCl_3$): δ = 3.12 – 3.08 (m, 2H, C5-H), 2.67 – 2.63 (m, 2H, C1-H), 2.42 – 2.40 (m, 2H, C2-H), 2.26 – 2.21 (m, 2H, C7-H_{exo}), 2.09 – 2.04 (m, 2H, C7-H_{endo}), 1.84 – 1.79 (m, 2H, C6-H_{endo}), 1.18 – 1.13 (m, 2H, C6-H_{exo}) ppm.

^{13}C NMR (150 MHz, $CDCl_3$): δ = 129.0 (C4), 70.6 (C3), 52.4 (C2), 49.8 (C5), 39.5 (C7), 30.2 (C1), 24.4 (C6) ppm.

IR (ATR): $\tilde{\nu}$ = 3015 (vw), 2950 (w), 2868 (w), 1733 (vw), 1590 (w), 1466 (w), 1442 (vw), 1403 (vw), 1370 (vw), 1333 (w), 1309 (vw), 1275 (vw), 1255 (vw), 1217 (vw), 1177 (w), 1161 (w), 1087 (w), 1050 (w), 1005 (w), 996 (m), 953 (m), 946 (m), 906 (w), 894 (vw), 882 (vw), 867 (w), 853 (vs), 839 (w), 817 (w), 805 (s), 788 (w), 735 (m), 723 (w), 654 (w), 625 (vw) cm^{-1}.

HRMS (EI): m/z for $C_{14}H_{14}Cl_4O^{+}$ $[M]^{+}$: calcd.: 337.9793
found: 337.9799.

1,4,12,13-Tetrachloropentacyclo[7.4.1.0^{4,12}.0^{5,14}.0^{6,11}]tetradecan-10-one (362)



358 **362**

To a solution of epoxide **358** (20.1 mg, 59.0 µmol, 1.00 eq.) in toluene (2.00 mL) was added a solution of triethylsilane in toluene (0.114 mL of a 10 vol-% solution, 70.8 µmol, 1.20 eq.) and $BF_3{\cdot}OEt_2$ (0.174 mL of a 5 vol-% solution in toluene, 70.8 µmol, 1.20 eq.). The reaction mixture was stirred at room temperature for 5 min and was then quenched by addition of saturated aqueous $NaHCO_3$ (1 mL). The reaction mixture was extracted with EtOAc (3 x 2 mL) and the combined organic layer was washed with brine (2 mL), dried (Na_2SO_4) and concentrated *in vacuo*. The residue was recrystallized from hexanes : Et_2O to afford ketone **362** (20 mg, 99%) as colorless crystals which were suitable for single crystal X-ray diffraction.

$C_{14}H_{14}Cl_4O$ M_r = 340.08 g·mol^{-1}.

TLC R_f = 0.20 (hexanes : EtOAc = 9 : 1).

mp 154 – 158 °C.

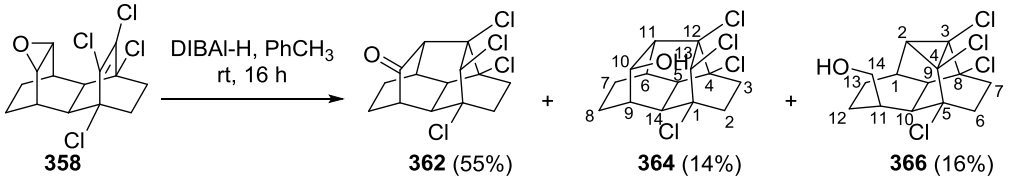
^{1}H NMR (600 MHz, $CDCl_3$): δ = 4.53 (d, $^4J_{C4\text{-}H,C13\text{-}Hanti}$ = 1.6 Hz, 1H, C4-H), 3.40 – 3.37 (m, 1H, C1-H), 3.23 (dd, $^3J_{C9\text{-}H,C8\text{-}H}$ = 6.4 Hz, $^4J_{C9\text{-}H,C1\text{-}H}$ = 2.9 Hz, 1H, C9-H), 2.85 – 2.82 (m, 2H, C7-H, C8-H), 2.78 (ddd, $^2J_{C14\text{-}Hsyn,C14\text{-}Hanti}$ = 14.1 Hz, $^3J_{C14\text{-}Hsyn,C13\text{-}Hsyn}$ = 10.9 Hz, $^3J_{C14\text{-}Hsyn,C13\text{-}Hanti}$ = 8.8 Hz, 1H, C14-H_{syn}), 2.68 – 2.63 (m, 2H, C2-H, C13-H_{syn}), 2.30 (ddd, $^2J_{C14\text{-}Hanti,C14\text{-}Hsyn}$ = 14.1 Hz, $^3J_{C14\text{-}Hanti,C13\text{-}Hanti}$ = 10.8 Hz, $^3J_{C14\text{-}Hanti,C13\text{-}Hsyn}$ = 0.8 Hz, 1H, C14-H_{anti}), 2.19 – 2.14 (m, 1H, C12-H_{syn}), 2.14 – 2.08 (m, 1H, C13-H_{anti}), 1.83 – 1.75 (m, 2H, C11-H_{syn}, C12-H_{anti}), 1.69 – 1.61 (m, 1H, C11-H_{anti}) ppm.

^{13}C NMR (150 MHz, $CDCl_3$): δ = 214.2 (C10), 78.0 (C6), 76.3 (C5), 72.8 (C4), 70.1 (C9), 69.1 (C3), 48.8 (C7), 48.6 (C2), 42.6 (C8), 40.3 (C1), 34.9 (C13), 30.6 (C14), 28.2 (C12), 17.7 (C11) ppm.

IR (ATR): $\tilde{\nu}$ = 2948 (w), 2870 (vw), 1729 (vs), 1463 (w), 1445 (vw), 1334 (vw), 1321 (vw), 1291 (vw), 1255 (vw), 1244 (vw), 1221 (vw), 1209 (vw), 1197 (vw), 1176 (vw), 1152 (vw), 1135 (vw), 1094 (w), 1084 (w), 1035 (vw), 1002 (s), 987 (w), 963 (vw), 931 (w), 921 (m), 892 (vs), 867 (w), 841 (w), 799 (w), 784 (vw), 758 (vw), 739 (w) cm^{-1}.

HRMS (EI): m/z for $C_{14}H_{14}Cl_4O^+$ $[M]^+$: calcd.: 337.9793
found: 337.9780.

Opening of 9,10-Epoxy-3,4,5,6-tetrachlorotetracyclo[6.2.2.2^{3,6}.0^{2,7}]tetradec-4-ene (358)



358 **362** (55%) **364** (14%) **366** (16%)

To a solution of epoxide **358** (100 mg, 0.295 mmol, 1.00 eq.) in toluene (10.0 mL) at 0 °C was added a solution of DIBAL-H in toluene (1 M, 0.354 mL, 0.354 mmol, 1.20 eq.). The resulting mixture was allowed to warm to room temperature and stirred at room temperature for an additional 16 h. The reaction was quenched by addition of H_2O (3 mL) and subsequent stirring at room temperature for 30 min. To the mixture 1 M HCl (3 mL) was added and the resulting mixture was stirred for an additional 30 min. The mixture was diluted with CH_2Cl_2 (30 mL) and the organic layer was separated, washed with H_2O (2 x 20 mL), dried (Na_2SO_4) and concentrated *in vacuo*. Purification of the residue by flash column chromatography (2 x 16 cm, silica, hexanes : EtOAc = 95 : 5 to 85 : 15, 8 mL) afforded rearranged ketone **362** (#31–44, 55 mg, 55%) as a colorless solid and alcohols **364** (#49-72, 14 mg, 14%) and **366** (#28-32, 16 mg, 16%) as colorless oils.

*1,4,12,13-Tetrachloropentacyclo[7.4.1.0^{4,12}.0^{5,14}.0^{6,11}]tetradecan-10-one (**362**)*

See above.

*1,4,12,13-Tetrachloro-10-exo-hydroxypentacyclo[7.4.1.0^{4,12}.0^{5,14}.0^{6,11}]tetradecane (**364**)*

$C_{14}H_{16}Cl_4O$ M_r = 342.09 g·mol^{-1}.

TLC R_f = 0.44 (hexanes : EtOAc = 9 : 1).

^{1}H NMR (600 MHz, $CDCl_3$): δ = 6.89 (d, $^4J_{C13\text{-}H,C2\text{-}Hendo}$ = 1.6 Hz, 1H, C13-H), 4.25 (d, $^3J_{C10\text{-}H,C11\text{-}H}$ = 6.0 Hz, 1H, C10-H), 3.00 (dddd, $^3J_{C11\text{-}H,C6\text{-}H}$ = 7.6 Hz, $^3J_{C11\text{-}H,C10\text{-}H}$ = 6.0 Hz, $^4J_{C11\text{-}H,C5\text{-}H}$ = 1.6 Hz, $^4J_{C11\text{-}H,C9\text{-}H}$ = 1.6 Hz, 1H, C11-H), 2.98 – 2.93 (m, 1H, C6-H), 2.87 (ddd, $^2J_{C3\text{-}Hexo,C3\text{-}Hendo}$ = 13.9 Hz, $^3J_{C3\text{-}Hexo,C2\text{-}Hexo}$ = 10.8 Hz, $^3J_{C3\text{-}Hexo,C2\text{-}Hendo}$ = 8.8 Hz, 1H, C3-H$_{exo}$), 2.64 (ddd, $^2J_{C2\text{-}Hexo,C2\text{-}Hendo}$ = 12.7 Hz, $^3J_{C2\text{-}Hexo,C3\text{-}Hexo}$ = 10.8 Hz, $^3J_{C2\text{-}Hexo,C3\text{-}Hendo}$ = 1.0 Hz, 1H, C2-H$_{exo}$), 2.49 – 2.42 (m, 2H, C5-H, C14-H), 2.33 (dddd, $^3J_{C9\text{-}H,C14\text{-}H}$ = 4.9 Hz, $^3J_{C9\text{-}H,C8\text{-}Hendo}$ = 1.6 Hz, $^3J_{C9\text{-}H,C8\text{-}Hexo}$ = 1.6 Hz, $^4J_{C9\text{-}H,C11\text{-}H}$ = 1.6 Hz, 1H, C9-H), 2.17 (ddd, $^2J_{C3\text{-}Hendo,C3\text{-}Hexo}$ = 13.9 Hz, $^3J_{C3\text{-}Hendo,C2\text{-}Hendo}$ = 10.7 Hz, $^3J_{C3\text{-}Hendo,C2\text{-}Hexo}$ = 1.0 Hz, 1H, C3-H$_{endo}$), 2.10 – 2.02 (m, 1H, C2-H$_{endo}$), 1.94 (dddd, $^2J_{C8\text{-}HA,C8\text{-}HB}$ = 12.8 Hz, $^3J_{C8\text{-}HA,C7\text{-}HA}$ = 10.0 Hz, $^3J_{C8\text{-}HA,C7\text{-}HB}$ = 5.2 Hz, $^3J_{C8\text{-}HA,C9\text{-}H}$ = 1.6 Hz, 1H, C8-H$_A$), 1.71 – 1.59 (m, 2H, C7-H), 1.44 – 1.36 (m, 1H, C8-H$_B$) ppm.

^{13}C NMR (150 MHz, $CDCl_3$): δ = 78.6 (C12), 77.7 (C4), 74.2 (C10), 70.2 (C13), 69.4 (C1), 58.2 (C11), 53.2 (C14), 50.1 (C5), 36.4 (C6), 36.1 (C9), 35.6 (C2), 31.1 (C3), 28.2 (C8), 18.4 (C7) ppm.

IR (ATR): $\tilde{\nu}$ = 3426 (vw), 3057 (w), 2948 (m), 2874 (w), 1719 (w), 1464 (m), 1446 (w), 1361 (vw), 1335 (m), 1319 (w), 1270 (w), 1255 (w), 1223 (w), 1208 (w), 1154 (vw), 1102 (m), 1087 (w), 1087 (w), 1061 (s), 1030 (w), 1019 (m), 1004 (vs), 983 (s), 972 (s), 934 (m), 908 (vs), 893 (vs), 855 (m), 832 (w), 816 (m), 800 (m), 780 (m), 750 (m), 733 (s) cm^{-1}.

HRMS (EI): m/z for $C_{14}H_{16}Cl_4O^+$ $[M]^+$: calcd.: 339.9950
found: 339.9947.

*3,4,5,8-Tetrachloro-11-hydroxymethylpentacyclo[7.4.0.0^{2,4}.0^{3,8}.0^{5,10}]tridecane (**366**)*

$C_{14}H_{16}Cl_4O$ M_r = 342.09 g·mol^{-1}.

TLC R_f = 0.12 (hexanes : EtOAc = 9 : 1).

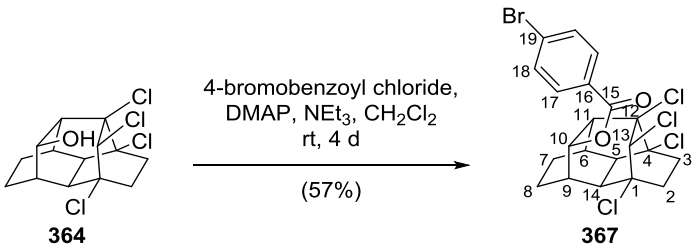
^{1}H NMR (600 MHz, $CDCl_3$): δ = 3.93 – 3.83 (m, 2H, C14-H), 2.95 – 2.92 (m, 1H, C2-H), 2.49 – 2.46 (m, 1H, C10-H), 2.44 – 2.22 (m, 4H, C1-H, C6-H_A, C7-H), 2.07 – 2.01 (m, 1H, C13-H_A), 1.97 (dd, $^3J_{C9\text{-}H,C1\text{-}H}$ = 2.2 Hz, $^4J_{C9\text{-}H,C2\text{-}H}$ = 2.2 Hz, 1H, C9-H), 1.90 – 1.83 (m, 1H, C6-H_B), 1.72 – 1.63 (m, 1H, C13-H_B), 1.62 – 1.51 (m, 3H, C11-H, C12-H) ppm.

^{13}C NMR (150 MHz, $CDCl_3$): δ = 74.9 (C5), 70.1 (C8), 66.5 (C14), 56.3 (C3), 52.7 (C4), 51.5 (C1), 46.1 (C11), 41.4 (C10), 41.1 (C9), 40.6 (C6), 34.5 (C2), 30.6 (C7), 26.9 (C13), 19.7 (C12) ppm.

IR (ATR): $\tilde{\nu}$ = 3363 (w), 2932 (m), 2867 (w), 1719 (vw), 1464 (m), 1446 (w), 1366 (w), 1349 (w), 1320 (w), 1298 (w), 1246 (w), 1230 (w), 1206 (w), 1167 (w), 1065 (w), 1049 (w), 1030 (vs), 1017 (vs), 971 (vs), 940 (w), 920 (vs), 908 (s), 891 (w), 797 (w), 732 (vs), 661 (vw) cm^{-1}.

HRMS (EI): m/z for $C_{14}H_{16}Cl_4O^+$ $[M]^+$: calcd.: 339.9950
found: 339.9934.

1,4,12,13-Tetrachloro-10-*exo*-hydroxypentacyclo[7.4.1.0^{4,12}.0^{5,14}.0^{6,11}]tetradecane *para*-bromobenzoate (367)



To a solution alcohol **364** (12.7 mg, 0.037 mmol, 1.00 eq.), DMAP (0.4 mg, 3.70 µmol, 0.100 eq.) and triethylamine (10 µL, 7.5 mg, 0.074 mmol, 2.00 eq.) in CH_2Cl_2 (1.50 mL) was added benzoyl chloride (12.2 mg, 0.056 mmol, 1.50 eq.) and the resulting mixture was stirred at room temperature for 96 h. The reaction mixture was concentrated *in vacuo*. Purification of the residue by flash column

chromatography (2 x 20 cm, silica, hexanes : EtOAc = 4 : 1, 8 mL, #9─12) afforded bromo benzoate **367** (11 mg, 57%) as a colorless solid. Recrystallization from CH_2Cl_2/hexanes afforded crystals suitable for single crystal X-ray diffraction.

$C_{21}H_{19}BrCl_4O_2$ M_r = 525.10 g·mol^{-1}.

TLC R_f = 0.64 (hexanes : EtOAc = 3 : 1).

mp 199 ─ 200 °C.

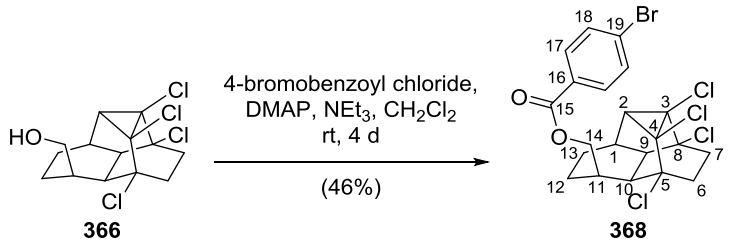
^{1}H NMR (400 MHz, $CDCl_3$): δ = 7.88 – 7.84 (m, 2H, C17-H), 7.68 – 7.62 (m, 2H, C18-H), 6.32 (d, $^4J_{C13\text{-}H,C2\text{-}Hendo}$ = 1.5 Hz, 1H, C13-H), 5.32 – 5.28 (m, 1H, C10-H), 3.24 (dddd, $^3J_{C11\text{-}H,C6\text{-}H}$ = 7.6 Hz, $^3J_{C11\text{-}H,C10\text{-}H}$ = 6.0 Hz, $^4J_{C11\text{-}H,C5\text{-}H}$ = 1.4 Hz, $^4J_{C11\text{-}H,C9\text{-}H}$ = 1.4 Hz, 1H, C11-H), 3.10 (dddd, $^3J_{C6\text{-}H,C11\text{-}H}$ = 7.6 Hz, $^3J_{C6\text{-}H,C5\text{-}H}$ = 4.0 Hz, $^3J_{C6\text{-}H,C7\text{-}H_A}$ = 2.0 Hz, $^3J_{C6\text{-}H,C7\text{-}H_B}$ = 2.0 Hz, 1H, C6-H), 2.89 (ddd, $^2J_{C3\text{-}Hexo,C3\text{-}Hendo}$ = 13.9 Hz, $^3J_{C3\text{-}Hexo,C2\text{-}Hexo}$ = 10.8 Hz, $^3J_{C3\text{-}Hexo,C2\text{-}Hendo}$ = 8.7 Hz, 1H, C3-H_{exo}), 2.66 (ddd, $^2J_{C2\text{-}Hexo,C2\text{-}Hendo}$ = 12.7 Hz, $^3J_{C2\text{-}Hexo,C3\text{-}Hexo}$ = 10.8 Hz, $^3J_{C2\text{-}Hexo,C3\text{-}Hendo}$ = 0.9 Hz, 1H, C2-H_{exo}), 2.57 – 2.47 (m, 3H, C5-H, C9-H, C14-H), 2.28 – 2.15 (m, 2H, C3-H_{endo}, C8-H_A), 2.08 (dddd, $^2J_{C2\text{-}Hendo,C2\text{-}Hexo}$ = 12.7 Hz, $^3J_{C2\text{-}Hendo,C3\text{-}Hendo}$ = 10.5 Hz, $^3J_{C2\text{-}Hendo,C3\text{-}Hexo}$ = 8.7 Hz, $^3J_{C2\text{-}Hendo,C13\text{-}H}$ = 1.5 Hz, 1H, C2-H_{endo}), 1.88 (dddd, $^2J_{C7\text{-}H_A,C7\text{-}H_B}$ = 14.8 Hz, $^3J_{C7\text{-}H_A,C8\text{-}H_A}$ = 10.6 Hz, $^3J_{C7\text{-}H_A,C8\text{-}H_B}$ = 8.2 Hz, $^3J_{C7\text{-}H_A,C6\text{-}H}$ = 2.0 Hz, 1H, C7-H_A), 1.74 (dddd, $^2J_{C7\text{-}H_B,C7\text{-}H_A}$ = 14.8 Hz, $^3J_{C7\text{-}H_B,C8\text{-}H_B}$ = 10.2 Hz, $^3J_{C7\text{-}H_B,C8\text{-}H_A}$ = 4.1 Hz, $^3J_{C7\text{-}H_B,C6\text{-}H}$ = 2.0 Hz, 1H, C7-H_B), 1.48 (dddd, $^2J_{C8\text{-}H_B,C8\text{-}H_A}$ = 13.0 Hz, $^3J_{C8\text{-}H_B,C7\text{-}H_B}$ = 10.2 Hz, $^3J_{C8\text{-}H_B,C7\text{-}H_A}$ = 8.2 Hz, $^3J_{C8\text{-}H_B,C9\text{-}H}$ = 1.5 Hz, 1H, C8-H_B) ppm.

^{13}C NMR (100 MHz, $CDCl_3$): δ = 164.8 (C15), 132.4 (C18), 131.2 (C17), 129.0 (C19), 128.5 (C16), 77.9 (C12), 77.3 (C1), 76.6 (C10), 70.7 (C13), 69.0 (C4), 57.1 (C11), 52.7 (C14), 50.2 (C5), 36.6 (C6), 35.3 (C2), 34.0 (C9), 31.1 (C3), 28.0 (C8), 18.5 (C7) ppm.

IR (ATR): $\tilde{\nu}$ = 3096 (vw), 2950 (w), 2877 (vw), 1721 (vs), 1590 (m), 1485 (w), 1464 (vw), 1399 (w), 1361 (vw), 1334 (vw), 1307 (w), 1270 (vs), 1254 (vs), 1225 (w), 1209 (vw), 1194 (vw), 1174 (w), 1150 (vw), 1112 (m), 1095 (vs), 1033 (w), 1010 (vs), 985 (w), 968 (vw), 958 (vw), 943 (vw), 912 (m), 898 (w), 882 (w), 860 (vw), 847 (w), 820 (w), 803 (w), 780 (vw), 755 (s), 733 (s), 682 (vw) cm^{-1}.

HRMS (ESI─): m/z for $C_{22}H_{20}BrCl_4O_4^+$ $[M+HCO_2^-]^-$: calcd.: 568.9275
found: 568.9279.

3,4,5,8-Tetrachloro-11-hydroxymethylpentacyclo[7.4.0.0^{2,4}.0^{3,8}.0^{5,10}]tridecane *para*-bromobenzoate (368)



366 **368**

To a solution alcohol **366** (12.7 mg, 0.037 mmol, 1.00 eq.), DMAP (0.4 mg, 3.70 µmol, 0.100 eq.) and triethylamine (10 µL, 7.5 mg, 0.074 mmol, 2.00 eq.) in CH_2Cl_2 (1.50 mL) was added benzoyl chloride (12.2 mg, 0.056 mmol, 1.50 eq.) and the resulting mixture was stirred at room temperature for 96 h. The reaction mixture was concentrated *in vacuo*. Purification of the residue by flash column chromatography (2 x 15 cm, silica, hexanes : EtOAc = 3 : 1, 8 mL, #12─15) afforded bromo benzoate **368** (9 mg, 46%) as a colorless solid. Recrystallization from CH_2Cl_2/hexanes afforded crystals suitable for single crystal X-ray diffraction.

$C_{21}H_{19}BrCl_4O_2$ M_r = 525.10 g·mol^{-1}.

TLC R_f = 0.71 (hexanes : EtOAc = 3 : 1).

mp 166 ─ 167 °C.

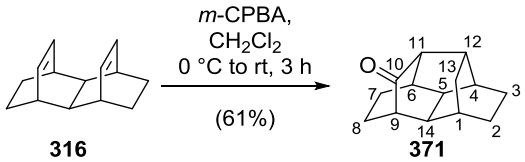
^{1}H NMR (400 MHz, $CDCl_3$): δ = 7.91 – 7.86 (m, 2H, C17-H), 7.61 – 7.56 (m, 2H, C18-H), 4.62 – 4.53 (m, 2H, C14-H), 2.97 – 2.91 (m, 1H, C2-H), 2.53 – 2.48 (m, 1H, C10-H), 2.48 – 2.22 (m, 4H, C1-H, C6-H_A, C7-H), 2.09 – 2.02 (m, 1H, C13-H_A), 1.99 (dd, $^3J_{C9\text{-}H,C1\text{-}H}$ = 2.6 Hz, $^4J_{C9\text{-}H,C2\text{-}H}$ = 1.8 Hz, 1H, C9-H), 1.92 – 1.83 (m, 1H, C6-H_B), 1.82 – 1.73 (m, 1H, C11-H), 1.73 – 1.65 (m, 3H, C12-H, C13-H_B) ppm.

^{13}C NMR (100 MHz, $CDCl_3$): δ = 165.9 (C15), 131.9 (C18), 131.2 (C17), 129.3 (C19), 128.3 (C16), 74.7 (C5), 69.4 (C8), 69.4 (C14), 56.2 (C3), 52.5 (C4), 51.4 (C1), 43.2 (C11), 42.8 (C10), 40.9 (C9), 40.5 (C6), 34.2 (C2), 30.5 (C7), 26.7 (C13), 20.3 (C12) ppm.

IR (ATR): $\tilde{\nu}$ = 2938 (vw), 2870 (vw), 1718 (vs), 1591 (w), 1484 (vw), 1464 (vw), 1398 (w), 1350 (vw), 1271 (vs), 1173 (w), 1114 (m), 1102 (m), 1069 (w), 1035 (vw), 1012 (m), 972 (w), 922 (w), 848 (vw), 798 (vw), 757 (m), 734 (vw), 683 (vw) cm^{-1}.

HRMS (ESI─): m/z for $C_{22}H_{20}BrCl_4O_4^+$ [M+HCO_2^-]$^-$: calcd.: 568.9275
found: 568.9279.

Pentacyclo[7.4.1.0^{4,12}.0^{5,14}.0^{6,11}]tetradecan-10-one (371)



To a solution of tetracyclotetradecadiene **316** (30.0 mg, 0.161 mmol, 1.00 eq.) in CH_2Cl_2 (2.50 mL) at 0 °C was added *m*-CPBA (70-75 wt%, 37.5 mg, 0.161 mmol, 1.00 eq.). The reaction mixture was stirred at 0 °C for 1 h, was then allowed to warm to room temperature and stirred at room temperature for an additional 2 h. After dilution with CH_2Cl_2 (15 mL) the reaction mixture was poured into 10% aqueous NaOH (10 mL) and the organic layer was washed with H_2O (2 x 7.5 mL), brine (7.5 mL), dried (Na_2SO_4) and concentrated *in vacuo*. Purification of the residue by flash column chromatography (1 x 13 cm, hexanes : EtOAc = 9 : 1, 8 mL, #4–5) afforded ketone **371** (20.0 mg, 61%) as a colorless solid. Recrystallization from hexanes afforded crystals suitable for X-ray analysis.

$C_{14}H_{18}O$ M_r = 202.29 g·mol^{-1}.

TLC R_f = 0.36 (hexanes : EtOAc = 9 : 1).

mp 95 – 97 °C.

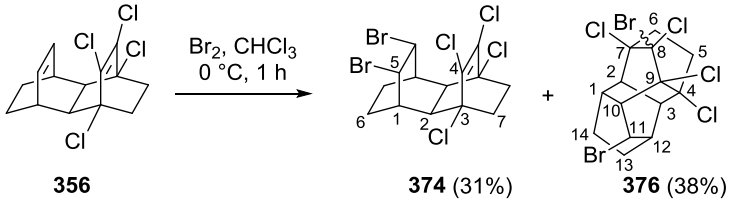
^{1}H NMR (300 MHz, $CDCl_3$): δ = 2.80 – 2.71 (m, 1H, C7-H), 2.40 – 2.29 (m, 1H, C12-H), 2.27 – 2.19 (m, 1H, C5-H), 2.17 – 2.10 (m, 1H, C14-H), 2.07 – 2.01 (m, 1H, C9-H), 2.00 – 1.88 (m, 2H, C6-H, C8-H_A), 1.85 – 1.72 (m, 4H, C4-H, C3-H_A,, C7-H_A, C8-H_B), 1.67 – 1.53 (m, 5H, C1-H, C2-H_A, C3-H_B, C7-H_B, C13-H_A), 1.52 – 1.37 (m, 2H, C2-H_B, C13-H_B) ppm.

^{13}C NMR (100 MHz, $CDCl_3$): δ = 222.7 (C8), 58.9 (C7), 47.1 (C9), 42.5 (C14), 40.6 (C6), 39.1 (C5), 38.3 (C4), 37.4 (C12), 29.5 (C1), 28.6 (C8), 28.3 (C13), 27.2 (C2), 19.8 (C3), 19.8 (C7) ppm.

IR (ATR): $\tilde{\nu}$ = 2925 (s), 2859 (m), 2250 (vw), 1721 (vs), 1476 (w), 1462 (w), 1442 (w), 1376 (vw), 1344 (vw), 1316 (vw), 1300 (w), 1292 (w), 1260 (s), 1216 (w), 1195 (w), 1166 (w), 1147 (w), 1090 (s), 1063 (s), 1025 (s), 994 (m), 972 (w), 954 (vw), 909 (m), 886 (m), 874 (w), 858 (m), 836 (w), 812 (vs), 798 (vs), 732 (vs), 690 (w), 674 (w), 642 (w), 622 (w) cm^{-1}.

HRMS (EI): m/z for $C_{14}H_{18}O^+$ [M^+]: calcd.: 202.1352
found: 202.1348.

Bromination of *syn*-3,4,5,6-Tetrachlorotetracyclo[6.2.2.2^{3,6}.0^{2,7}]tetradeca-4,9-diene (356)



356 **374** (31%) **376** (38%)

To a solution of chlorinated diene **356** (40.5 mg, 125 µmol, 1.00 eq.) in $CHCl_3$ (2.50 mL) at 0 °C was added a solution of bromine in $CHCl_3$ (0.700 mL of a 1.37 vol-% solution, 188 µmol, 1.50 eq.). The reaction mixture was stirred at 0 °C for 1 h and the reaction was then quenched by addition of diluted aqueous $Na_2S_2O_3$. The organic layer was separated and the aqueous layer was extracted with $CHCl_3$ (3 x 5 mL). The combined organic layer was washed with saturated aqueous $NaHCO_3$ (10 mL), brine (10 mL), dried (Na_2SO_4) and concentrated *in vacuo*. Purification of the residue by flash column chromatography (2 x 18 cm, hexanes : EtOAc = 95 : 5, 8 mL) afforded 1,2-dibromide **374** (#16–20, 19 mg, 31%) as a colorless solid and hexahalogenated tritwistane **376** (#24–29, 23 mg, 38%) as an unseparable mixture of isomers at C8 (7 : 3 in favor of the displayed isomer) in form of a colorless solid. Recrystallization from hexanes (for 1,2-dibromide **374**) and $CHCl_3$ (for halogenated tritwistane **376**) respectively afforded crystals suitable for X-ray diffraction experiments.

*syn-9,10-Dibromo-3,4,5,6-tetrachlorotetracyclo[6.2.2.2^{3,6}.0^{2,7}]tetradec-4-ene (**374**)*

$C_{14}H_{14}Br_2Cl_4$ M_r = 483.88 g·mol^{-1}.

TLC R_f = 0.43 (hexanes : EtOAc = 9 : 1).

mp 152 – 155 °C.

^{1}H NMR (300 MHz, $CDCl_3$): δ = 4.58 – 4.51 (m, 2H, C5-H), 2.56 – 2.50 (m, 2H, C2-H), 2.44 – 2.40 (m, 2H, C1-H), 2.40 – 2.34 (m, 2H, C6-H$_{endo}$), 2.26 – 2.18 (m, 2H, C7-H$_{exo}$), 2.13 – 2.04 (m, 2H, C7-H$_{endo}$), 1.48 – 1.40 (m, 2H, C6-H$_{exo}$) ppm.

^{13}C NMR (75 MHz, $CDCl_3$): δ = 129.4 (C4), 69.3 (C3), 52.9 (C2), 50.4 (C5), 39.6 (C7), 35.7 (C1), 21.2 (C6) ppm.

IR (ATR): $\tilde{\nu}$ = 2956 (w), 2937 (w), 2874 (w), 1727 (vw), 1591 (w), 1465 (m), 1444 (vw), 1374 (vw), 1360 (vw), 1328 (w), 1311 (m), 1261 (w), 1203 (w), 1176 (w), 1094 (w), 1059 (m), 1019 (w), 1008 (w), 991 (s), 956 (vs), 905 (s), 877 (m), 866 (w), 837 (m), 811 (s), 761 (w), 734 (vs), 713 (m), 684 (w), 661 (s), 610 (m) cm^{-1}.

HRMS (EI): m/z for $C_{14}H_{14}Br_2Cl_4^+$ $[M]^+$: calcd.: 479.8211
found: 479.8209.

*8,11-Dibromopentacyclo[8.4.0.0^{2,7}.0^{3,12}.0^{4,9}]tetradecane (**376**)*

$C_{14}H_{14}Br_2Cl_4$ M_r = 483.88 g·mol^{-1}.

TLC R_f = 0.34 (hexanes : EtOAc = 9 : 1).

mp 210 °C (dec.).

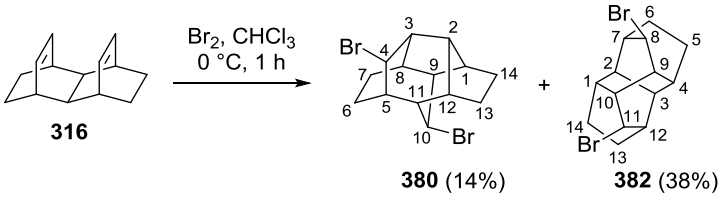
^{1}H NMR (300 MHz, $CDCl_3$, both diastereomers): δ = 5.54 (d, $^3J_{C11\text{-}H,C12\text{-}H}$ = 5.8 Hz, 1H, C11-H), 3.27 – 3.19 (m, 1H, C12-H*), 3.06 – 2.91 (m, 2H, C3-H*, C13-H_A**), 2.68 – 2.24 (m, 6H, C1-H*, C2-H*, C10-H*, C13-H_B**, C14-H**), 2.14 – 1.91 (m, 2H, C5-H), 1.63 – 1.42 (m, 2H, C6-H) ppm.

^{13}C NMR (75 MHz, $CDCl_3$, major diastereomer): δ = 91.6 (C4*), 81.2 (C7*), 73.3 (C8*), 71.9 (C9*), 56.5 (C1**), 50.6 (C2**), 48.0 (C3**), 47.4 (C11), 36.5 (C5***), 35.7 (C6***), 33.3 (C10**), 26.6 (C12**), 21.2 (C13***), 19.9 (C14***) ppm.

IR (ATR): $\tilde{\nu}$ = 2959 (w), 2928 (w), 2874 (vw), 2851 (vw), 1730 (vw), 1463 (m), 1448 (w), 1362 (vw), 1344 (vw), 1329 (w), 1300 (w), 1295 (w), 1281 (vw), 1261 (w), 1242 (w), 1203 (vw), 1172 (w), 1147 (vw), 1110 (w), 1094 (w), 1080 (w), 1061 (vw), 1034 (w), 1018 (m), 1007 (w), 984 (w), 959 (w), 945 (vs), 906 (s), 866 (m), 849 (m), 839 (m), 816 (w), 806 (s), 791 (s), 773 (w), 738 (m), 680 (w), 667 (vs), 649 (s), 642 (s), 603 (s) cm^{-1}.

HRMS (EI): m/z for $C_{14}H_{14}Br_2Cl_4^+$ $[M]^+$: calcd.: 479.8211
found: 479.8203.

Bromination of *syn*-3,4,5,6-Tetracyclo[6.2.2.2^{3,6}.0^{2,7}]tetradeca-4,9-diene (316)



To a solution of diene **316** (49.9 mg, 268 µmol, 1.00 eq.) in $CHCl_3$ (3.00 mL) at 0 °C was added a solution of bromine in $CHCl_3$ (1.253 mL of a 1.37 vol-% solution, 335 µmol, 1.25 eq.). The reaction mixture was stirred at 0 °C for 1 h and the reaction was then quenched by addition of diluted aqueous $Na_2S_2O_3$. The organic layer was separated and the aqueous layer was extracted with $CHCl_3$ (3 x 15 mL). The combined organic layer was washed with saturated aqueous $NaHCO_3$ (30 mL), brine (30 mL), dried (Na_2SO_4) and concentrated *in vacuo*. Purification of the residue by flash column chromatography (2 x 18 cm, hexanes : Et_2O = 95 : 5, 8 mL) afforded rearranged dibromide **380** (#21–25, 15 mg, 14%) and dibromotritwistane **382** (#27–39, 35 mg, 38%) as colorless solids. Recrystallization from hexanes afforded crystals suitable for X-ray diffraction experiments for both compounds.

*4,10-Dibromopentacyclo[7.5.0.0^{2,12}.0^{3,8}.0^{5,11}]tetradecane (**380**)*

$C_{14}H_{18}Br_2$ M_r = 346.10 g·mol^{-1}.

TLC R_f = 0.35 (hexanes).

mp 130 – 136 °C.

^{1}H NMR (600 MHz, $CDCl_3$): δ = 5.12 (m, 1H, C10-H), 4.78 (ddd, $^3J_{C4\text{-}H,C5\text{-}H}$ = 5.4 Hz, $^3J_{C4\text{-}H,C3\text{-}H}$ = 5.4 Hz, $^4J_{C4\text{-}H,C6\text{-}Hanti}$ = 1.3 Hz, 1H, C4-H), 2.82 – 2.79 (m, 1H, C3-H), 2.79 – 2.74 (ddd, $^2J_{C14\text{-}Hsyn,C14\text{-}Hanti}$ = 13.5 Hz, $^3J_{C14\text{-}Hsyn,C13\text{-}Hsyn}$ = 9.6 Hz, $^3J_{C14\text{-}Hsyn,C13\text{-}Hanti}$ = 4.4 Hz, 1H, C14-H_{syn}), 2.52 – 2.46 (m, 2H, C2-H, C11-H), 2.43 – 2.38 (m, 2H, C8-H, C13-H_{syn}), 2.38 – 2.31 (m, 4H, C1-H, C5-H, C9-H, C12-H), 2.27 (dddd, $^2J_{C6\text{-}Hsyn,C6\text{-}Hanti}$ = 14.4 Hz, $^3J_{C6\text{-}Hsyn,C7\text{-}Hsyn}$ = 11.4 Hz, $^3J_{C6\text{-}Hsyn,C7\text{-}Hanti}$ = 4.7 Hz, $^3J_{C6\text{-}Hsyn,C5\text{-}H}$ = 1.9 Hz, 1H, C6-H_{syn}), 2.11 (dddd, $^2J_{C7\text{-}Hsyn,C7\text{-}Hanti}$ = 14.9 Hz, $^3J_{C7\text{-}Hsyn,C6\text{-}Hsyn}$ = 11.4 Hz, $^3J_{C7\text{-}Hsyn,C6\text{-}Hanti}$ = 6.0 Hz, $^3J_{C7\text{-}Hsyn,C8\text{-}H}$ = 6.0 Hz, 1H, C7-H_{syn}), 1.83 – 1.76 (m, 2H, C6-H_{anti}, C13-H_{anti},), 1.75 – 1.68 (m, 1H, C14-H_{anti}), 1.56 – 1.53 (m, 1H, C7-H_{anti}) ppm.

^{13}C NMR (150 MHz, $CDCl_3$): δ = 56.3 (C4), 53.2 (C10), 52.9 (C2), 51.9 (C9), 47.3 (C1), 47.0 (C11), 43.1 (C3), 41.5 (C8), 38.0 (C5), 37.2 (C12), 28.9 (C13), 26.9 (C14), 24.0 (C6), 18.8 (C7) ppm.

IR (ATR): $\tilde{\nu}$ = 2933 (vs), 2861 (w), 1477 (w), 1460 (vw), 1444 (vw), 1296 (w), 1270 (vw), 1238 (w), 1188 (w), 973 (w), 923 (vw), 874 (w), 823 (m), 803 (m), 770 (m), 741 (m), 719 (m), 662 (vw) cm^{-1}.

HRMS (EI): m/z for $C_{14}H_{18}Br^+$ [M–Br]$^+$: calcd.: 265.0586
found: 265.0594.

*8,11-Dibromopentacyclo[8.4.0.0^{2,7}.0^{3,12}.0^{4,9}]tetradecane (**382**)*

$C_{14}H_{18}Br_2$ M_r = 346.10 g·mol^{-1}.

TLC R_f = 0.25 (hexanes).

^{1}H NMR (600 MHz, $CDCl_3$): δ = 4.63 (d, $^3J_{C11\text{-}H,C12\text{-}H}$ = 5.9 Hz, 1H, C11-H), 4.49 (d, $^3J_{C8\text{-}H,C9\text{-}H}$ = 5.4 Hz, 1H, C8-H), 2.67 – 2.63 (m, 1H, C1-H), 2.50 – 2.46 (m, 1H, C10-H), 2.43 – 2.38 (m, 1H, C9-H), 2.33 – 2.26 (m, 1H, C14-H_{endo}), 2.18 – 2.12 (m, 2H, C3-H*, C12-H), 2.02 – 1.95 (m, 2H, C4-H, C13-H_{endo}), 1.82 – 1.76 (m, 2H, C2-H, C6-H_{endo}), 1.73 – 1.66 (m, 2H, C5-H_{endo}, C7-H*,), 1.61 – 1.52 (m, 2H, C6-H_{exo}, C13-H_{exo},), 1.48 – 1.38 (m, 2H, C5-H_{exo}, C14-H_{exo}) ppm.

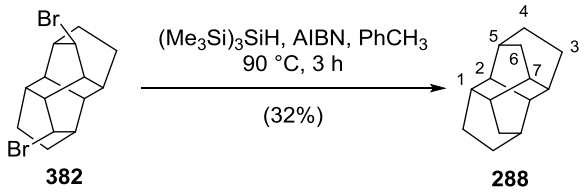
^{13}C NMR (150 MHz, $CDCl_3$): δ = 56.0 (C11), 54.9 (C8), 42.3 (C9), 39.8 (C10), 37.8 (C3*), 37.7 (C7*), 36.1 (C2), 35.6 (C12), 32.3 (C4), 27.5 (C1), 25.9 (C6), 21.5 (C5), 21.4 (C14), 21.2 (C13) ppm.

IR (ATR): $\tilde{\nu}$ = 2939 (vs), 2868 (m), 1462 (w), 1446 (vw), 1332 (vw), 1301 (vw), 1294 (vw), 1285 (vw), 1273 (w), 1237 (w), 1196 (vw), 1036 (vw), 982 (vw), 964 (vw), 922

(w), 908 (vw), 900 (vw), 880 (vw), 856 (vw), 826 (w), 799 (vw), 765 (vw), 755 (w), 745 (m) cm^{-1}.

HRMS (EI): m/z for $C_{14}H_{18}Br_2^+$ $[M]^+$: calcd.: 345.9750
found: 345.9568.

Pentacyclo[8.4.0.0^{2,7}.0^{3,12}.0^{4,9}]tetradecane – *C*$_2$-Tritwistane (288)



382 **288**

To a solution of dibromide **382** (34.6 mg, 0.100 mmol, 1.00 eq.) in toluene (3.00 mL) was added TTMSS (0.075 mL, 59.7 mg, 0.240 mmol, 2.40 eq.) and one crystal of AIBN (2.50 mg, 0.015 mmol, 0.150 eq.). The resulting mixture was heated to 90 °C for 3 h and was then allowed to cool to room temperature and was concentrated *in vacuo*. The residue was purified by flash column chromatography (2 x 20 cm, *n*-pentane, 8 mL, #8) to afford tritwistane (**288**) contaminated with some silicon species as a colorless oil. A solution of this oil in $CDCl_3$ (1.50 mL) was stirred over a fluoride polymer at room temperature for 8 d. The solution was filtered over a short silica column and the solvent was removed *in vacuo* to afford tritwistane (**288**) (6 mg, 32%) as a waxy amorphous solid.

$C_{14}H_{20}$ M_r = 188.31 g·mol^{-1}.

TLC R_f = 0.92 (hexanes).

^{1}H NMR (600 MHz, $CDCl_3$): δ = 1.72 (m, 2H, C7-H), 1.70 – 1.63 (m, 6H, C5-H, C1-H, C3-H_A), 1.52 – 1.44 (m, 10H, C2-H, C6-H_A, C4-H, C3-H_B), 1.36 (dd, $^2J_{C6\text{-}H_B,C6\text{-}H_A}$ = 12.1 Hz, $^3J_{C6\text{-}H_B,C7\text{-}H}$ = 5.0 Hz, 2H, C6-H_B) ppm.

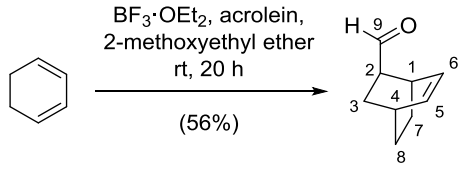
^{13}C NMR (150 MHz, $CDCl_3$): δ = 35.4 (C2), 33.6 (C7), 29.1 (C5), 28.6 (C1), 27.3 (C6), 24.8 (C4), 22.8 (C3) ppm.

IR (ATR): $\tilde{\nu}$ = 2921 (vs), 2908 (vs), 2871 (m), 2860 (m), 1476 (vw), 1456 (vw), 1445 (vw), 1333 (vw), 1293 (vw), 1242 (vw), 1211 (vw), 1042 (vw), 915 (vw), 838 (vw) cm^{-1}.

HRMS (EI): m/z for $C_{14}H_{20}^+$ $[M]^+$: calcd.: 188.1560
found: 188.1549.

7.2 Synthetic Studies Toward Polytwistane

Bicyclo[2.2.2]oct-5-ene-2-*endo*-carbaldehyde (416)



243 **416**

To a solution of cyclohexadiene **243** (7.00 mL, 6.01 g, 75.0 mmol, 1.00 eq.) in 2-methoxyethyl ether (75.0 mL) at room temperature was added successively acrolein (25.0 mL, 21.0 g, 375 mmol, 5.00 eq.) and $BF_3 \cdot OEt_2$ (1.39 mL, 1.60 g, 11.3 mmol, 0.150 eq.). The reaction mixture was stirred at room temperature for 20 h. The mixture was diluted with H_2O (90 mL) and the aqueous layer was extracted with Et_2O (3 x 90 mL). The combined organic layer was washed with H_2O (3 x 90 mL), dried (Na_2SO_4) and concentrated *in vacuo*. Purification of the residue by flash column chromatography (5 x 25 cm, silica, *n*-pentane : Et_2O = 95 : 5, 100 mL, #12–19) afforded bicycloaldehyde **416** (5.68 g, 56%) as a colorless oil.

$C_9H_{12}O$ $M_r = 136.19\ g \cdot mol^{-1}$.

TLC $R_f = 0.59$ (*n*-pentane : Et_2O = 95 : 5).

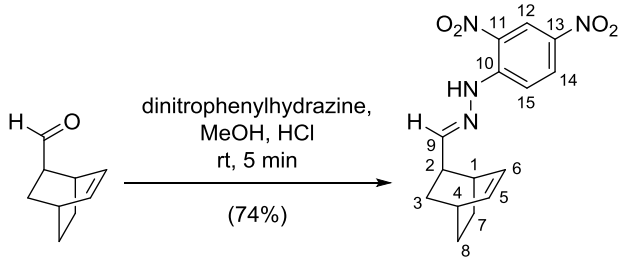
^{1}H NMR (300 MHz, $CDCl_3$): δ = 9.43 (d, $^3J_{C9\text{-}H,C2\text{-}H} = 1.6$ Hz, 1H, C9-H), 6.31 (ddd, $^3J_{C5\text{-}H,C6\text{-}H} = 8.0$ Hz, $^3J_{C5\text{-}H,C4\text{-}H} = 6.6$ Hz, $^4J_{C5\text{-}H,C1\text{-}H} = 1.2$ Hz, 1H, C5-H), 6.09 (ddd, $^3J_{C6\text{-}H,C5\text{-}H} = 8.0$ Hz, $^3J_{C6\text{-}H,C1\text{-}H} = 6.4$ Hz, $^4J_{C6\text{-}H,C4\text{-}H} = 1.2$ Hz, 1H, C6-H), 2.98 – 2.89 (m, 1H, C1-H), 2.68 – 2.59 (m, 1H, C4-H), 2.59 – 2.50 (m, 1H, C2-H), 1.77 – 1.47 (m, 4H, C3-H, C7-H_{syn}, C8-H_{syn}), 1.40 – 1.19 (m, 2H, C7-H_{anti}, C8-H_{anti}) ppm.

^{13}C NMR (75 MHz, $CDCl_3$): δ = 204.3 (C9), 136.4 (C5), 131.0 (C6), 51.2 (C2), 31.0 (C1), 29.5 (C4), 27.0 (C3), 25.5 (C7), 25.1 (C8) ppm.

IR (ATR): $\tilde{\nu}$ = 3795 (vw), 3424 (vw), 3046 (vw), 2940 (m), 2867 (w), 2810 (vw), 2707 (vw), 1721 (vs), 1615 (vw), 1466 (vw), 1453 (vw), 1415 (vw), 1392 (vw), 1373 (w), 1348 (vw), 1312 (vw), 1286 (vw), 1230 (vw), 1208 (vw), 1175 (w), 1159 (w), 1120 (vw), 1094 (vw), 1068 (w), 1038 (vw), 1015 (vw), 952 (w), 922 (m), 850 (w), 816 (w), 700 (vs), 606 (vw) cm^{-1}.

HRMS (EI): m/z for $C_9H_{12}O^+$ $[M]^+$: calcd.: 136.0883
found: 136.0886.

Bicyclo[2.2.2]oct-5-ene-2-*endo*-carbaldehyde 2,4-dinitrophenylhydrazone (417)



416 **417**

Dinitrophenylhydrazine (198 mg, 1.00 mmol, 1.00 eq.) was dissolved in a mixture of MeOH (15.0 mL) and concentrated HCl (1.00 mL) by slight warming. To this mixture aldehyde **416** (136 mg, 1.00 mmol, 1.00 eq.) was added and the resulting mixture was stirred at room temperature for 5 min. The resulting orange precipitate was filtered off, washed with MeOH and dried *in vacuo* to afford the desired hydrazine **417** (235 mg, 74%) as an orange solid. Recrystallization from EtOH afforded crystals suitable for single crystal X-ray diffraction.

$C_{15}H_{16}N_4O_4$ M_r = 316.31 g·mol^{-1}.

TLC R_f = 0.30 (hexanes:EtOAc = 9:1).

mp 161 – 163 °C.

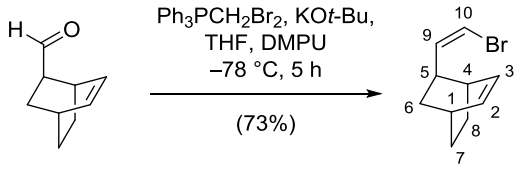
^{1}H NMR (300 MHz, $CDCl_3$): δ = 10.91 (s, 1H, N-H), 9.10 (d, $^4J_{C12\text{-}H,C14\text{-}H}$ = 2.6 Hz, 1H, C12-H), 8.28 (ddd, $^3J_{C14\text{-}H,C15\text{-}H}$ = 9.6 Hz, $^4J_{C14\text{-}H,C12\text{-}H}$ = 2.6 Hz, $^5J_{C14\text{-}H,N\text{-}H}$ = 0.8 Hz, 1H, C14-H), 7.88 (d, $^3J_{C15\text{-}H,C14\text{-}H}$ = 9.6 Hz, 1H, C15-H), 7.22 (d, $^3J_{C9\text{-}H,C2\text{-}H}$ = 6.2 Hz, 1H, C9-H), 6.44 – 6.36 (m, 1H, C5-H), 6.23 – 6.14 (m, 1H, C6-H), 2.85 – 2.75 (m, 1H, C2-H), 2.75 – 2.69 (m, 1H, C1-H), 2.69 – 2.61 (m, 1H, C4-H), 1.90 (ddd, $^2J_{C3\text{-}Hexo,C3\text{-}Hendo}$ = 12.5 Hz, $^3J_{C3\text{-}Hexo,C2\text{-}H}$ = 9.6 Hz, $^3J_{C3\text{-}Hexo,C4\text{-}H}$ = 2.7 Hz, 1H, C3-H_{exo}), 1.76 – 1.20 (m, 5H, C3-H_{endo}, C7-H, C8-H) ppm.

^{13}C NMR (75 MHz, $CDCl_3$): δ = 157.2 (C9), 145.3 (C10), 137.8 (C13), 136.3 (C5), 131.3 (C6), 130.0 (C14), 128.9 (C11), 123.7 (C12), 116.7 (C15), 41.5 (C2), 34.0 (C1), 30.9 (C3), 29.6 (C4), 25.8 (C7), 24.6 (C8) ppm.

IR (ATR): $\tilde{\nu}$ = 3288 (vw), 3107 (vw), 2936 (vw), 2864 (vw), 2361 (vw), 2341 (vw), 1739 (vw), 1616 (s), 1593 (w), 1509 (m), 1425 (vw), 1374 (vw), 1328 (vs), 1307 (s), 1289 (m), 1266 (m), 1217 (w), 1142 (m), 1083 (w), 1073 (w), 1046 (vw), 1024 (vw), 926 (w), 912 (vw), 863 (vw), 844 (vw), 834 (w), 764 (vw), 745 (w), 722 (w), 702 (m), 686 (vw), 668 (vw), 649 (vw), cm^{-1}.

HRMS (ESI–): m/z for $C_{15}H_{15}N_4O_4^-$ [M–H]$^-$: calcd.: 315.1099
found: 315.1096.

5-(*endo*-(*Z*)-2-Bromoalkenyl)bicyclo[2.2.2]oct-2-ene (418)



416 **418**

To a solution of (bromomethyl)triphenylphosphonium bromide (22.6 g, 51.8 mmol, 1.10 eq.) in THF (214 mL) was added KO*t*-Bu (5.81 g, 51.8 mmol, 1.10 eq.) at −78 °C. The resulting yellow reaction mixture was stirred at −78 °C for 15 min, after which time DMPU (26.7 mL, 28.4 g, 221 mmol, 4.70 eq.) and aldehyde **416** (6.41 g, 47.1 mmol, 1.00 eq.) were added successively. The mixture was stirred for an additional 4 h at −78 °C, then diluted with hexanes (600 mL) and filtered over celite. The residue was washed with hexanes (600 mL) and the combined filtrates were concentrated *in vacuo*. Purification of the residue by flash column chromatography (5 x 16 cm, silica, hexanes : EtOAc = 100 : 1, 100 mL, #3–5) afforded alkenyl bromide **418** (7.3 g, 73%) as a colorless oil.

$C_{10}H_{13}Br$ M_r = 213.11 g·mol^{-1}.

TLC R_f = 0.69 (hexanes).

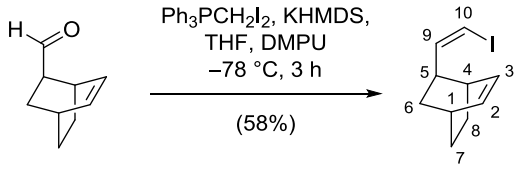
^{1}H NMR (300 MHz, $CDCl_3$): δ = 6.38 – 6.30 (m, 1H, C2-H), 6.19 – 6.11 (m, 1H, C3-H), 5.96 (dd, $^3J_{C10\text{-}H,C9\text{-}H}$ = 6.9 Hz, $^4J_{C10\text{-}H,C5\text{-}H}$ = 1.0 Hz, 1H, C10-H), 5.81 (dd, $^3J_{C9\text{-}H,C5\text{-}H}$ = 9.0 Hz, $^3J_{C9\text{-}H,C10\text{-}H}$ = 6.9 Hz, 1H, C9-H), 2.91 – 2.78 (m, 1H, C5-H), 2.58 – 2.51 (m, 1H, C1-H), 2.51 – 2.44 (m, 1H, C4-H), 1.93 (ddd, $^2J_{C6\text{-}Hexo,C6\text{-}Hendo}$ = 12.5 Hz, $^3J_{C6\text{-}Hexo,C5\text{-}H}$ = 9.6 Hz, $^3J_{C6\text{-}Hexo,C1\text{-}H}$ = 2.6 Hz, 1H, C6-H_{exo}), 1.69– 1.57 (m, 1H, C8-H_{anti}), 1.54 – 1.45 (m, 1H, C7-H_{anti}), 1.31 – 1.18 (m, 2H, C7-H_{syn}, C8-H_{syn}), 1.05 – 0.94 (m, 1H, C6-H_{endo}) ppm.

^{13}C NMR (75 MHz, $CDCl_3$): δ = 141.7 (C9), 135.8 (C2), 132.1 (C3), 104.7 (C10), 38.8 (C5), 34.4 (C4), 33.8 (C6), 29.8 (C1), 25.9 (C8), 24.5 (C7) ppm.

IR (ATR): $\tilde{\nu}$ = 3043 (vw), 2936 (m), 2864 (w), 2361 (vw), 1739 (vw), 1681 (vw), 1616 (w), 1464 (vw), 1451 (vw), 1374 (w), 1350 (vw), 1323 (w), 1290 (w), 1277 (m), 1239 (vw), 1201 (vw), 1162 (vw), 1092 (vw), 1041 (vw), 942 (w), 913 (w), 858 (w), 842 (vw), 816 (vw), 805 (w), 767 (vw), 699 (vs), 670 (m), 644 (s), 627 (m) cm^{-1}.

HRMS (EI): m/z for $C_{10}H_{13}Br^+$ $[M]^+$: calcd.: 212.0195
found: 212.0197.

5-(*endo*-(*Z*)-2-Iodoalkenyl)bicyclo[2.2.2]oct-2-ene (419)



416 **419**

To a suspension of (iodomethyl)triphenylphosphonium iodide (4.67 g, 8.80 mmol, 1.10 eq.) in THF (35.0 mL) at 0 °C was added a solution of KHMDS (1.00 m in THF, 8.80 mL, 8.80 mmol, 1.10 eq.). The resulting yellow reaction mixture was stirred at 0 °C for 5 min, after which time the mixture was cooled to −78 °C and DMPU (4.53 mL, 4.82 g, 37.6 mmol, 4.70 eq.) and a solution of aldehyde **416** (1.09 g, 8.00 mmol, 1.00 eq.) in THF (24.0 mL) were added successively. The mixture was stirred for 3 h at −78 °C and was then diluted with hexanes (110 mL) and filtered over celite. The residue was washed with hexanes (330 mL) and the combined filtrates were concentrated *in vacuo*. Purification of the residue by flash column chromatography (4 x 15 cm, silica, hexanes : EtOAc = 100 : 1, 20 mL, #14–20) afforded alkenyl iodide **419** (1.21 g, 58%) as a colorless oil.

$C_{10}H_{13}I$ M_r = 260.12 g·mol^{-1}.

TLC R_f = 0.87 (hexanes : EtOAc = 9 : 1).

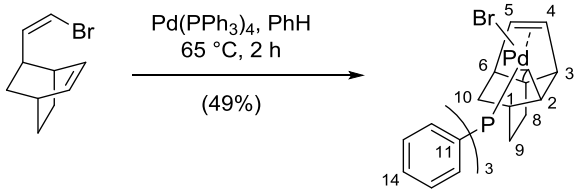
^{1}H NMR (300 MHz, $CDCl_3$): δ = 6.37 – 6.30 (m, 1H, C2-H), 6.18 – 6.10 (m, 1H, C3-H), 5.99 (dd, $^3J_{C10\text{-}H,C9\text{-}H}$ = 7.2 Hz, $^4J_{C10\text{-}H,C5\text{-}H}$ = 0.8 Hz, 1H, C10-H), 5.87 (dd, $^3J_{C9\text{-}H,C5\text{-}H}$ = 8.7 Hz, $^3J_{C9\text{-}H,C10\text{-}H}$ = 7.2 Hz, 1H, C9-H), 2.71 – 2.60 (m, 1H, C5-H), 2.60 – 2.51 (m, 1H, C1-H), 2.51 – 2.43 (m, 1H, C4-H), 1.94 (ddd, $^2J_{C6\text{-}Hexo,C6\text{-}Hendo}$ = 12.4 Hz, $^3J_{C6\text{-}Hexo,C5\text{-}H}$ = 9.6 Hz, $^3J_{C6\text{-}Hexo,C1\text{-}H}$ = 2.7 Hz, 1H, C6-H_{exo}), 1.70 – 1.57 (m, 1H, C8-H_{anti}), 1.57 – 1.46 (m, 1H, C7-H_{anti}), 1.35 – 1.16 (m, 2H, C7-H_{syn}, C8-H_{syn}), 1.00 (dddd, $^2J_{C6\text{-}Hendo,C6\text{-}Hexo}$ = 12.4, $^3J_{C6\text{-}Hendo,C5\text{-}H}$ = 4.7 Hz, $^3J_{C6\text{-}Hendo,C1\text{-}H}$ = 2.9 Hz, $^4J_{C6\text{-}Hendo,C7\text{-}Hsyn}$ = 2.9 Hz, 1H, C6-H_{endo}) ppm.

^{13}C NMR (75 MHz, $CDCl_3$): δ = 148.0 (C9), 135.8 (C2), 132.2 (C3), 78.9 (C10), 43.7 (C5), 34.4 (C4), 33.5 (C6), 29.8 (C1), 25.9 (C8), 24.5 (C7) ppm.

IR (ATR): $\tilde{\nu}$ = 3042 (vw), 2935 (s), 2863 (m), 1719 (vw), 1604 (w), 1572 (vw), 1463 (vw), 1450 (vw), 1374 (vw), 1348 (vw), 1338 (vw), 1319 (w), 1289 (vw), 1268 (vs), 1238 (w), 1197 (vw), 1176 (vw), 1156 (vw), 1119 (vw), 1085 (vw), 1058 (vw), 1039 (vw), 1026 (vw), 1014 (vw), 998 (vw), 972 (vw), 948 (vw), 932 (vw), 912 (w), 857 (w), 838 (vw), 814 (vw), 801 (w), 712 (vs), 699 (vs), 660 (m), 636 (w), 610 (s) cm^{-1}.

HRMS (EI): m/z for $C_{10}H_{13}I^+$ $[M]^+$: calcd.: 260.0056
found: 260.0064.

Tricyclo[4.3.1.0^{3,7}]dec-4-ene-2-yltriphenylphosphinepalladium(II) bromide (420)



418 **420**

To a solution of $Pd(PPh_3)_4$ (497 mg, 0.430 mmol, 1.00 eq.) in benzene (3.00 mL) was added (*Z*)-alkenyl bromide **418** (91.6 mg, 0.430 mmol, 1.00 eq.) by syringe. The yellow reaction mixture was heated to 65 °C for 2 h. The mixture was allowed to cool to room temperature and Et_2O (50 mL) was added, precipitating a white solid. The precipitate was filtered off and the filtrate was allowed to stand. Upon slow evaporation of the solvent the title palladium complex **420** (122 mg, 49%) crystallized in the form of yellow platelets. Crystals suitable for single crystal X-ray diffraction could be obtained from this mixture.

$C_{28}H_{28}BrPPd$ M_r = 581.82 g·mol^{-1}.

mp 148 °C (dec.).

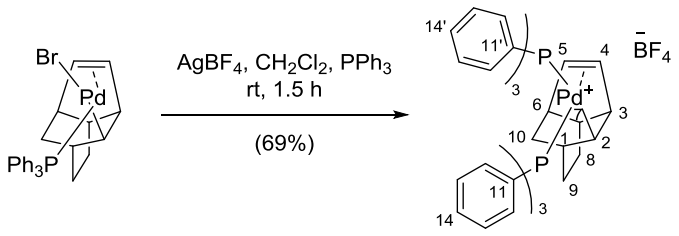
^{1}H NMR (600 MHz, $CDCl_3$): δ = 7.74 – 7.68 (m, 6H, C12-H), 7.44 – 7.36 (m, 9H, C13-H, C14-H), 6.91 – 6.86 (m, 1H, C5-H), 6.19 – 6.15 (m, 1H, C4-H), 3.13 – 3.05 (m, 1H, C3-H), 2.90 – 2.82 (m, 1H, C10-H_{syn}), 2.56 – 2.49 (m, 1H, C6-H), 2.21 – 2.14 (m, 1H, C7-H), 1.74 (dd, $^2J_{C10\text{-}Hanti,C10\text{-}Hsyn}$ = 13.0 Hz, $^3J_{C10\text{-}Hanti,C6\text{-}H}$ = 8.1 Hz, 1H, C10-H_{anti}), 1.60 – 1.49 (m, 2H, C8-H), 1.44 – 1.35 (m, 1H, C9-H_A), 1.25 – 1.22 (m, 1H, C1-H), 1.02 – 0.90 (m, 2H, C2-H, C9-H_A) ppm.

^{13}C NMR (150 MHz, $CDCl_3$): δ = 134.6 (d, $^2J_{C12,P}$ = 12.3 Hz, C12), 133.4 (d, $^2J_{C5,P}$ = 9.8 Hz, C5), 131.2 (d, $^1J_{C11,P}$ = 43.8 Hz, C11), 130.7 (d, $^4J_{C14,P}$ = 2.4 Hz, C14), 128.5 (d, $^3J_{C13,P}$ = 10.4 Hz, C13), 87.0 (d, $^2J_{C4,P}$ = 13.0 Hz, C4), 48.7 (s, C3), 46.3 (s, C7), 41.4 (d, $^3J_{C6,P}$ = 2.4 Hz, C6), 33.1 (s, C10), 31.9 (s, C1), 30.1 (d, $^4J_{C9,P}$ = 5.1 Hz, C9), 26.9 (d, $^2J_{C2,P}$ = 7.9 Hz, C2), 18.1 (s, C8) ppm.

IR (ATR): $\tilde{\nu}$ = 3056 (vw), 2924 (vs), 2857 (s), 1735 (vw), 1463 (vw), 1451 (vw), 1442 (vw), 1333 (m), 1308 (vw), 1298 (vw), 1288 (vw), 1272 (vw), 1260 (vw), 1234 (vw), 1209 (vw), 1184 (vw), 1144 (vw), 1104 (vw), 1084 (vw), 1054 (vw), 1028 (vw), 1002 (vw), 977 (w), 958 (vw), 928 (vw), 910 (m), 834 (vw), 822 (vw), 808 (w), 784 (vw), 765 (vw), 747 (vw), 731 (m), 701 (vw), 684 (vw), 668 (vw) cm^{-1}.

HRMS (ESI+): m/z for $C_{28}H_{28}PPd^+$ $[M–Br]^+$: calcd.: 501.0958
found: 501.0962.

Tricyclo[4.3.1.0^{3,7}]dec-4-ene-2-ylbistriphenylphosphinepalladium(II) tetrafluoroborate (421)



420 **421**

A mixture of palladium complex **420** (79.7 mg, 0.137 mmol, 1.00 eq.), $AgBF_4$ (26.7 mg, 0.137 mmol, 1.00 eq.) and PPh_3 (35.9 mg, 0.137 mmol, 1.00 eq.) in CH_2Cl_2 (15.0 mL) was stirred at room temperature for 1.5 h and was then filtered. Et_2O (15.0 mL) was added to the filtrate and the mixture was allowed to stand to facilitate crystallization. Silver bromide deposited on the bottom of the flask. The supernatant solution was decanted and concentrated *in vacuo*. Crystallization of the residue from CH_2Cl_2/Et_2O afforded yellow crystals of complex **421** (80 mg, 69%) that were suitable for single crystal X-ray diffraction.

$C_{46}H_{43}BF_4P_2Pd$ M_r = 851.02 g·mol^{-1}.

TLC R_f = 0.43 (CH_2Cl_2 : MeOH = 95 : 5).

mp 117 °C (dec.).

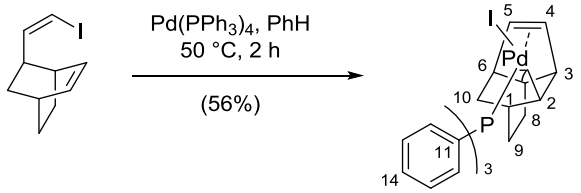
^{1}H NMR (600 MHz, $CDCl_3$): δ = 7.51 – 7.44 (m, 6H, C12-H), 7.43 – 7.35 (m, 6H, C14-H, C14'-H), 7.34 – 7.27 (m, 12H, C13-H, C13'-H), 7.13 – 7.07 (m, 6H, C12'-H), 5.99 – 5.92 (m, 1H, C4-H), 5.82 – 5.74 (m, 1H, C5-H), 3.53 – 3.43 (m, 1H, C3-H), 2.73 – 2.64 (m, 1H, C10-H_A), 2.49 – 2.41 (m, 1H, C6-H), 2.32 – 2.22 (m, 1H, C7-H), 1.97 – 1.87 (m, 1H, C10-H_B), 1.60 – 1.50 (m, 2H, C8-H), 1.49 – 1.40 (m, 1H, C9-H_A), 1.40 – 1.33 (m, 1H, C1-H), 1.29 – 1.20 (m, 1H, C2-H), 0.97 – 0.86 (m, 1H, C9-H_B) ppm.

^{13}C NMR (150 MHz, $CDCl_3$): δ = 134.3 (d, $^2J_{C12,P}$ = 12.4 Hz, C12), 133.5 (d, $^2J_{C12,P}$ = 12.4 Hz, C12'), 131.6 (s, C14), 130.8 (s, C14'), 130.4 (d, $^1J_{C11,P}$ = 30.4 Hz, C11), 129.5 (d, $^1J_{C11,P}$ = 30.4 Hz, C11'), 129.3 (d, $^3J_{C13,P}$ = 8.6 Hz, C13), 129.1 (C5), 129.0 (d, $^3J_{C13,P}$ = 8.6 Hz, C13'), 90.0 (br s, C4), 47.8 (s, C7), 47.0 (s, C3), 41.1 (s, C6), 33.1 (s, C10), 31.9 (s, C1), 30.9 (br s, C9), 29.9 (br s, C2), 17.9 (s, C8) ppm.

IR (ATR): $\tilde{\nu}$ = 3059 (vw), 2926 (w), 2860 (vw), 1481 (w), 1434 (m), 1335 (vw), 1310 (vw), 1279 (vw), 1189 (vw), 1160 (vw), 1094 (s), 1056 (vs), 998 (vw), 742 (m), 695 (vs) cm^{-1}.

HRMS (ESI+): m/z for $C_{28}H_{28}PPd^+$ [M–PPh_3–BF_4]$^+$: calcd.: 501.0958
found: 501.0960.

Tricyclo[4.3.1.0^{3,7}]dec-4-ene-2-yltriphenylphosphinepalladium(II) iodide (424)



419 **424**

To a solution of $Pd(PPh_3)_4$ (497 mg, 0.430 mmol, 1.00 eq.) in benzene (3.00 mL) was added (*Z*)-alkenyl iodide **419** (112 mg, 0.430 mmol, 1.00 eq.). The yellow reaction mixture was heated to 50 °C for 2 h. The mixture was allowed to cool to room temperature and Et_2O (25 mL) was added, precipitating a white solid. The precipitate was filtered off and the filtrate was allowed to stand. Upon slow evaporation of the solvent the title palladium complex **424** (150 mg, 56%) crystallized in the form of yellow platelets. Crystals suitable for single crystal X-ray diffraction could be obtained from this mixture.

$C_{28}H_{28}IPPd$ $M_r = 628.83\ g{\cdot}mol^{-1}$.

TLC $R_f = 0.49$ (hexanes : EtOAc = 3 : 1).

mp 136 °C (dec.).

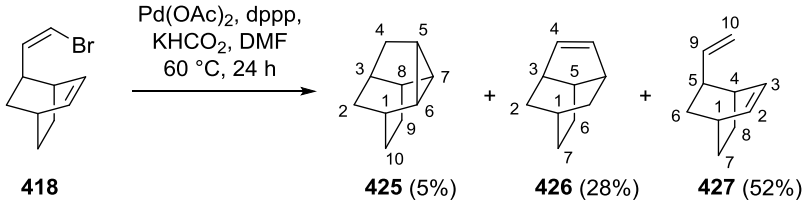
^{1}H NMR (600 MHz, $CDCl_3$): δ = 7.72 – 7.65 (m, 6H, C12-H), 7.41 – 7.36 (m, 9H, C13-H, C14-H), 7.20 – 7.11 (m, 1H, C5-H), 6.05 – 5.96 (m, 1H, C4-H), 3.21 – 3.11 (m, 1H, C3-H), 2.87 – 2.82 (m, 1H, C10-H_{syn}), 2.56 – 2.49 (m, 1H, C6-H), 2.25 – 2.18 (m, 1H, C7-H), 1.71 (dd, $^2J_{C10\text{-}Hanti,C10\text{-}Hsyn}$ = 13.1 Hz, $^3J_{C10\text{-}Hanti,C6\text{-}H}$ = 8.1 Hz, 1H, C10-H_{anti}), 1.63 – 1.50 (m, 2H, C8-H), 1.46 – 1.38 (m, 1H, C9-H_A), 1.33 – 1.27 (m, 1H, C1-H), 1.17 – 1.07 (m, 1H, C2-H), 1.00 – 0.92 (m, 1H, C9-H_B) ppm.

^{13}C NMR (150 MHz, $CDCl_3$): δ = 134.9 (d, $^2J_{C12,P}$ = 12.1 Hz, C12), 131.6 (br s, C5), 131.3 (d, $^1J_{C11,P}$ = 44.0 Hz, C11), 130.7 (d, $^4J_{C14,P}$ = 2.3 Hz, C14), 128.5 (d, $^3J_{C13,P}$ = 10.5 Hz, C13), 84.7 (br s, C4), 48.5 (s, C3), 46.9 (s, C7), 41.2 (s, C6), 32.2 (s, C1), 31.9 (s, C10), 30.5 (s, C9), 28.7 (br s, C2), 18.0 (s, C8) ppm.

IR (ATR): $\tilde{\nu}$ = 3047 (vw), 2956 (vw), 2930 (w), 2898 (vw), 2886 (vw), 2854 (vw), 1479 (vw), 1434 (m), 1331 (vw), 1307 (vw), 1299 (vw), 1287 (vw), 1275 (vw), 1262 (vw), 1187 (vw), 1178 (vw), 1090 (m), 1076 (vw), 1033 (vw), 998 (w), 981 (w), 908 (vw), 805 (vw), 758 (m), 743 (s), 703 (m), 694 (vs), 688 (s) cm^{-1}.

HRMS (ESI+): m/z for $C_{28}H_{28}PPd^+$ $[M–I]^+$: calcd.: 501.0958
found: 501.0959.

Cyclization of Alkenyl Bromide 418 with Catalytic Amounts of Palladium



To a round bottom flask were added $Pd(OAc)_2$ (106 mg, 0.470 mmol 0.100 eq.), 1,3-bis(diphenylphosphino)propane (236 mg, 0.940 mmol, 0.200 eq.) and potassium formate (1.19 g, 14.1 mmol, 3.00 eq.). The flask was evacuated and refilled with argon three times. The salts were dissolved in degassed DMF (250 mL) and alkenyl bromide **418** (1.00 g, 4.70 mmol, 1.00 eq.) was added. The reaction mixture was transferred to a preheated oil bath and stirred at 60 °C for 24 h. During the reaction the color of the mixture turned from yellow to black. The reaction mixture was allowed to cool to room temperature and was diluted with H_2O (200 mL) and pentane (200 mL) and the resulting mixture was stirred for 15 min at room temperature. The organic layer was separated and the aqueous layer was extracted with *n*-pentane (3 x 50 mL). The combined organic layer was dried (Na_2SO_4) and concentrated *in vacuo* (at room temperature). Purification of the residue by flash column chromatography (4 x 30 cm, silica, *n*-pentane, 20 mL) afforded cyclopropane **425** as a colorless solid (#14, 33 mg, 5%), isotwistene **426** (#15, 196 mg, 28%) as a colorless solid and vinyl bicyclooctene **427** (#16–19, 400 mg, 52%) as a colorless oil.

*Tetracyclo[4.4.0.0^{3,8}.0^{5,7}]decane (**425**)*

$C_{10}H_{14}$	M_r = 134.22 g·mol^{-1}.
TLC	R_f = 0.88 (hexanes).
mp	117 – 121 °C.
^{1}H NMR	(600 MHz, $CDCl_3$): δ = 2.06 – 2.01 (m, 1H, C8-H), 1.97 – 1.92 (m, 1H, C1-H), 1.81 – 1.76 (m, 2H, C3-H, C4-H_A), 1.70 – 1.64 (m, 1H, C9-H_A), 1.63 – 1.56 (m, 1H, C9-H_B), 1.50 – 1.43 (m, 2H, C4-H_B, C10-H_A), 1.42 – 1.35 (m, 1H, C10-H_B), 1.29 – 1.22 (m, 2H, C2-H_A, C5-H), 1.15 – 1.07 (m, 2H, C2-H_B, C7-H), 0.80 – 0.74 (m, 1H, C6-H) ppm.
^{13}C NMR	(150 MHz, $CDCl_3$): δ = 35.6 (C4), 33.2 (C3), 33.1 (C8), 33.0 (C2), 27.4 (C10), 25.1 (C1), 19.6 (C9), 18.4 (C5), 17.1 (C7), 16.3 (C6) ppm.
IR	(ATR): $\tilde{\nu}$ = 3035 (vw), 2928 (vs), 2861 (s), 1472 (vw), 1459 (vw), 1342 (vw), 1318 (vw), 1305 (vw), 907 (vw), 888 (vw), 778 (w), 752 (w), 735 (w), 710 (vw), 668 (vw) cm^{-1}.
HRMS	(EI): m/z for $C_{10}H_{14}^+$ $[M]^+$: calcd.: 134.1090 found: 134.1087.

*Tricyclo[4.3.1.0^{3,7}]dec-4-ene – Isotwistene (**426**)*

$C_{10}H_{14}$ M_r = 134.22 g·mol^{-1}.

TLC R_f = 0.82 (hexanes).

mp 96 – 98 °C.

^{1}H NMR (600 MHz, $CDCl_3$): δ = 6.10 – 6.07 (m, 2H, C4-H), 2.29 – 2.24 (m, 2H, C3-H), 2.09 – 2.05 (m, 1H, C5-H), 1.83 – 1.77 (m, 3H, C1-H, C6-H), 1.58 – 1.54 (m, 2H, C7-H), 1.47 – 1.36 (m, 4H, C2-H) ppm.

^{13}C NMR (75 MHz, $CDCl_3$): δ = 140.2 (C4), 40.3 (C5), 39.4 (C3), 29.7 (C2), 28.5 (C1), 28.4 (C7), 19.7 (C6) ppm.

IR (ATR): $\tilde{\nu}$ = 3053 (vw), 2924 (s), 2856 (s), 1646 (vw), 1597 (vw), 1468 (vw), 1450 (w), 1345 (w), 1300 (vw), 1207 (vw), 1156 (vw), 1103 (vw), 1042 (vw), 1025 (vw), 966 (w), 907 (w), 819 (w), 785 (w), 726 (vs), 668 (vw) cm^{-1}.

HRMS (EI): m/z for $C_{10}H_{14}^+$ $[M]^+$: calcd.: 134.1090
found: 134.1097.

*5-endo-Vinylbicyclo[2.2.2]oct-2-ene (**427**)*

$C_{10}H_{14}$ M_r = 134.22 g·mol^{-1}.

TLC R_f = 0.75 (hexanes).

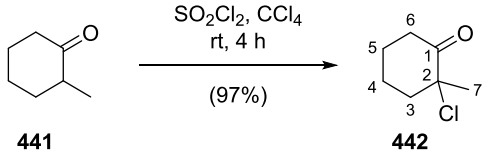
^{1}H NMR (300 MHz, $CDCl_3$): δ = 6.32 (ddd, $^3J_{C2\text{-}H,C3\text{-}H}$ = 7.9 Hz, $^3J_{C2\text{-}H,C1\text{-}H}$ = 6.6 Hz, $^4J_{C2\text{-}H,C6\text{-}H}$ = 1.1 Hz, 1H, C2-H), 6.22 – 6.14 (m, 1H, C3-H), 5.61 (ddd, $^3J_{C9\text{-}H,C10\text{-}Hanti}$ = 17.2 Hz, $^3J_{C9\text{-}H,C10\text{-}Hsyn}$ = 10.1 Hz, $^3J_{C9\text{-}H,C5\text{-}H}$ = 8.1 Hz, 1H, C9-H), 4.92 (ddd, $^3J_{C10\text{-}Hanti,C9\text{-}H}$ = 17.2 Hz, $^2J_{C10\text{-}Hanti,C10\text{-}Hsyn}$ = 2.0 Hz, $^4J_{C10\text{-}Hanti,C5\text{-}H}$ = 1.1 Hz, 1H, C10-H_{anti}), 4.83 (ddd, $^3J_{C10\text{-}Hsyn,C9\text{-}H}$ = 10.1 Hz, $^2J_{C10\text{-}Hsyn,C10\text{-}Hanti}$ = 2.0 Hz, $^4J_{C10\text{-}Hsyn,C5\text{-}H}$ = 0.9 Hz, 1H, C10-H_{syn}), 2.57 – 2.51 (m, 1H, C1-H), 2.51 – 2.44 (m, 1H, C4-H), 2.44 – 2.37 (m, 1H, C5-H), 1.82 (ddd, $^2J_{C6\text{-}Hexo,C6\text{-}Hendo}$ = 12.4 Hz, $^3J_{C6\text{-}Hexo,C5\text{-}H}$ = 9.5 Hz, $^3J_{C6\text{-}Hexo,C1\text{-}H}$ = 2.7 Hz, 1H, C6-H_{exo}), 1.66 – 1.44 (m, 2H, C7-H_{anti}, C8-H_{anti}), 1.41 – 1.23 (m, 2H, C7-H_{syn}, C8-H_{syn}), 1.16 – 1.04 (m, 1H, C6-H_{endo}) ppm.

^{13}C NMR (75 MHz, $CDCl_3$): δ = 145.6 (C9), 135.0 (C2), 132.2 (C3), 111.8 (C10), 42.6 (C5), 35.9 (C4), 33.8 (C6), 30.0 (C1), 26.3 (C8), 24.6 (C7) ppm.

IR (ATR): $\tilde{\nu}$ = 3044 (vw), 2927 (s), 2861 (m), 1638 (vw), 1450 (vw), 1419 (vw), 1374 (vw), 1345 (vw), 1300 (vw), 1176 (vw), 1103 (vw), 1043 (vw), 1025 (vw), 994 (w), 966 (vw), 906 (s), 857 (w), 819 (w), 785 (vw), 751 (vw), 727 (s), 708 (vs), 676 (w), 668 (w) cm^{-1}.

HRMS (EI): m/z for $C_{10}H_{14}^+$ $[M]^+$: calcd.: 134.1090
found: 134.1092.

2-Chloro-2-methylcyclohexanone (442)



441 **442**

To a solution of cyclohexanone **441** (50.0 mL, 46.2 g, 412 mmol, 1.00 eq.) in CCl_4 (260 mL) at room temperature was added a solution of sulfuryl chloride (36.7 mL, 61.2 g, 453 mmol, 1.10 eq.) in CCl_4 (60 mL) over a period of 2 h. After complete addition the reaction mixture was stirred at room temperature for an additional 2 h. The mixture was washed with H_2O (3 x 60 mL), saturated aqueous $NaHCO_3$ (2 x 50 mL), brine (50 mL) and dried ($MgSO_4$). The solvent was removed by distillation using a vigreux column at ambient pressure. The desired product **442** (58.3 g, 97%) was obtained as a yellow oil by distillation of the residue under reduced pressure (350 mbar, 50 °C).

$C_7H_{11}ClO$ M_r = 146.62 g·mol^{-1}.

TLC R_f = 0.65 (hexanes : EtOAc = 9 : 1).

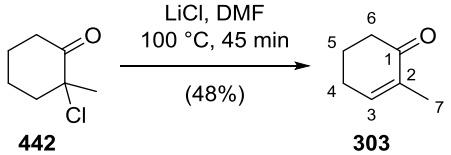
^{1}H NMR (300 MHz, $CDCl_3$): δ = 3.07 – 2.91 (m, 1H, C6-H_A), 2.34 – 2.22 (m, 2H, C3-H_A, C6-H_B), 2.12 – 1.93 (m, 2H, C4-H_A, C5-H_A), 1.90 – 1.76 (m, 1H, C3-H_B), 1.73 – 1.64 (m, 1H, C4-H_B), 1.63 – 1.58 (m, 1H, C5-H_B), 1.58 (s, 3H, C7-H) ppm.

^{13}C NMR (75 MHz, $CDCl_3$): δ = 205.1 (C1), 70.5 (C2), 43.0 (C3), 37.0 (C6), 27.1 (C5), 26.7 (C7), 21.5 (C4) ppm.

IR (ATR): $\tilde{\nu}$ = 2939 (w), 2868 (vw), 1720 (vs), 1448 (w), 1429 (w), 1379 (w), 1350 (vw), 1339 (vw), 1314 (vw), 1286 (vw), 1181 (vw), 1142 (w), 1124 (w), 1114 (w), 1088 (w), 1022 (vw), 989 (w), 938 (vw), 904 (vw), 868 (w), 843 (vw), 818 (w), 786 (vw), 764 (vw), 722 (vw), 675 (vw) cm^{-1}.

HRMS (EI): m/z for $C_7H_{11}ClO^+$ $[M]^+$: calcd.: 146.0493
found: 146.0494.

2-Methylcyclohex-2-enone (303)



442 **303**

A solution of 2-chloro-2-methylcyclohexanone (**442**) (58.6 g, 400 mmol, 1.00 eq.) and LiCl (10.4 g, 245 mmol, 0.613 eq.) in DMF (100 mL) was heated to 100 °C for 45 min. The reaction mixture was allowed to cool to room temperature and was diluted with Et_2O (400 mL). To this mixture was added H_2SO_4 (2.5 vol-%, 400 mL) to hydrolyze DMF and the resulting mixture was stirred at room

temperature for 4 h. The aqueous layer was separated, saturated with NaCl and extracted with Et_2O (4 x 60 mL, 2 x 100 mL). The combined organic layer was washed with brine (150 mL), saturated aqueous $NaHCO_3$ (150 mL), dried (Na_2SO_4) and concentrated *in vacuo*. Purification of the residue by distillation (30 mbar, 74 °C) afforded cyclohexenone **303** (20.9 g, 48%) as a colorless oil.

$C_7H_{10}O$ M_r = 110.16 g·mol^{-1}.

TLC R_f = 0.39 (hexanes : EtOAc = 9 : 1).

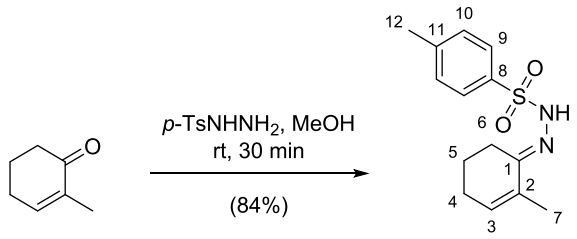
^{1}H NMR (300 MHz, $CDCl_3$): δ = 6.74 – 6.69 (m, 1H, C3-H), 2.42 – 2.36 (m, 2H, C6-H), 2.34 – 2.25 (m, 2H, C4-H), 2.01 – 1.90 (m, 2H, C5-H), 1.74 (dd, $^4J_{C7\text{-}H,C3\text{-}H}$ = 3.4 Hz, $^5J_{C7\text{-}H,C4\text{-}H}$ = 1.9 Hz, 3H, C7-H) ppm.

^{13}C NMR (75 MHz, $CDCl_3$): δ = 200.0 (C1), 145.7 (C3), 135.8 (C2), 38.4 (C6), 26.1 (C4), 23.4 (C5), 16.1 (C7) ppm.

IR (ATR): $\tilde{\nu}$ = 2948 (w), 2925 (w), 2889 (vw), 2869 (vw), 1722 (vw), 1665 (vs), 1453 (w), 1432 (w), 1419 (w), 1388 (w), 1359 (m), 1320 (vw), 1256 (vw), 1174 (w), 1139 (w), 1106 (m), 1082 (w), 1022 (w), 955 (vw), 902 (w), 880 (w), 860 (vw), 801 (vw), 708 (w), 685 (w) cm^{-1}.

HRMS (EI): m/z for $C_7H_{10}O^+$ $[M]^+$: calcd.: 110.0726
found: 110.0725.

2-Methylcyclohex-2-enone tosylhydrazone (443)



303 **443**

To a solution of tosylhydrazide (34.2 g, 184 mmol, 1.01 eq.) in MeOH (136 mL) was added a solution of ketone **303** (20 g, 182 mmol, 1.00 eq.) in MeOH (20 mL). The resulting mixture was stirred at room temperature for 30 min and was then allowed to stand at room temperature for 20 h to allow crystallization. Crystallization was completed by cooling to 0 °C for 1 h and the precipitate was collected by filtration and was washed with cold MeOH (40 mL) and dried *in vacuo* to afford hydrazone **443** (42.3 g, 84%) as a colorless solid.

$C_{14}H_{18}N_2O_2S$ M_r = 278.38 g·mol^{-1}.

TLC R_f = 0.37 (hexanes : EtOAc = 3 : 1).

mp 156 – 158 °C.

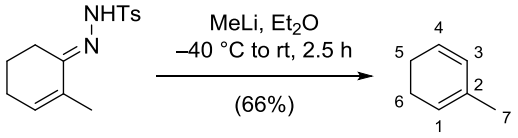
^{1}H NMR (300 MHz, $CDCl_3$): δ = 7.90 – 7.84 (m, 2H, C9-H), 7.51 (br s, 1H, N-H), 7.33 – 7.27 (m, 2H, C10-H), 6.09 – 6.03 (m, 1H, C3-H), 2.42 (s, 3H, C12-H), 2.28 – 2.21 (m, 2H, C6-H), 2.14 – 2.05 (m, 2H, C4-H), 1.80 – 1.76 (m, 3H, C7-H), 1.76 – 1.70 (m, 2H, C5-H) ppm.

^{13}C NMR (75 MHz, $CDCl_3$): δ = 154.8 (C1), 144.1 (C11), 135.4 (C8), 134.5 (C3), 132.7 (C2), 129.5 (C10), 128.4 (C9), 24.8 (C4), 24.3 (C6), 21.7 (C12), 21.4 (C5), 18.1 (C7) ppm.

IR (ATR): $\tilde{\nu}$ = 3179 (m), 2953 (vw), 2928 (vw), 1636 (vw), 1589 (vw), 1597 (vw), 1494 (vw), 1450 (vw), 1428 (vw), 1403 (w), 1332 (s), 1304 (w), 1292 (w), 1276 (vw), 1250 (vw), 1185 (vw), 1159 (vs), 1125 (w), 1092 (m), 1040 (w), 1022 (m), 1016 (m), 963 (vw), 921 (s), 895 (w), 881 (m), 860 (w), 812 (s), 738 (vs), 694 (s), 666 (s) cm^{-1}.

HRMS (EI): m/z for $C_{14}H_{18}N_2O_2S^+$ $[M]^+$: calcd.: 278.1083
found: 278.1077.

2-Methyl-1,3-cyclohexadiene (444)



443 **444**

To a solution of tosylhydrazone **443** (42.3 g, 152 mmol, 1.00 eq.) in Et_2O (200 mL) at –40 °C was added a solution of MeLi·LiBr (1.26 m in Et_2O, 241 mL, 304 mmol, 2.00 eq.) over 2 h in 25 mL aliquots. The resulting yellow solution was stirred at –40 °C for an additional 15 min, was then allowed to warm to room temperature and stirred at this temperature for 15 min. The reaction mixture was cooled to 0 °C and the reaction was quenched by addition of H_2O (35 mL). The mixture was filtered and the residue was washed with Et_2O (100 mL). The combined organic layer was washed with NH_4Cl (2 x 35 mL). The combined aqueous layer was re-extracted with Et_2O (2 x 25 mL). The combined organic layer was dried (Na_2SO_4) and the solvent was removed by distillation through a vigreux column. The desired product **444** (9.5 g, 66%) was obtained in the residue of the distillation as a colorless oil contaminated with Et_2O.

C_7H_{10} M_r = 94.15 g·mol^{-1}.

TLC R_f = 0.92 (hexanes).

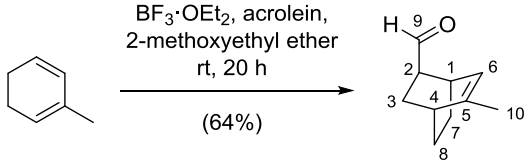
^{1}H NMR (400 MHz, $CDCl_3$): δ = 5.85 – 5.76 (m, 2H, C3-H, C4-H), 5.51 – 5.46 (m, 1H, C1-H), 2.13 – 2.04 (m, 4H, C5-H, C6-H), 1.76 – 1.71 (m, 3H, C7-H) ppm.

^{13}C NMR (100 MHz, $CDCl_3$): δ = 131.6 (C2), 128.3 (C3*), 126.6 (C4*), 120.6 (C1), 22.6 (C5*), 22.4 (C6*), 21.5 (C7) ppm.

IR (ATR): $\tilde{\nu}$ = 3414 (br, vw), 3025 (vw), 2933 (m), 2870 (w), 1713 (vw), 1669 (vw), 1604 (vw), 1495 (vw), 1438 (m), 1400 (w), 1377 (m), 1358 (m), 1323 (w), 1291 (w), 1242 (w), 1183 (w), 1105 (m), 1048 (vs), 1026 (vs), 996 (s), 978 (vs), 952 (vs), 902 (m), 880 (s), 854 (m), 785 (m), 750 (m), 730 (vs), 695 (s), 663 (w) cm^{-1}.

HRMS (EI): m/z for $C_7H_{10}^+$ $[M]^+$: calcd.: 94.0777
found: 94.0779.

5-Methylbicyclo[2.2.2]oct-5-ene-2-*endo*-carbaldehyde (445)



444 **445**

To a solution of methylcyclohexadiene **444** (4.54 mL, 3.77 g, 40.0 mmol, 1.00 eq.) in 2-methoxyethyl ether (20.0 mL) at room temperature was added successively acrolein (4.00 mL, 3.36 g, 60.0 mmol, 1.50 eq.) and $BF_3{\cdot}Et_2O$ (0.740 mL, 0.852 g, 6.00 mmol, 0.300 eq.). The reaction mixture was stirred at room temperature for 20 h. The mixture was diluted with H_2O (50 mL) and the aqueous layer was extracted with Et_2O (3 x 50 mL). The combined organic layer was washed with H_2O (3 x 50 mL), dried (Na_2SO_4) and concentrated *in vacuo*. Purification of the residue by flash column chromatography (5 x 20 cm, silica, *n*-pentane : Et_2O = 95 : 5, 100 mL, #19–25) afforded bicycloaldehyde **445** (3.83 g, 64%) as a colorless oil.

$C_{10}H_{14}O$ M_r = 150.22 $g{\cdot}mol^{-1}$.

TLC R_f = 0.62 (hexanes : EtOAc = 9 : 1).

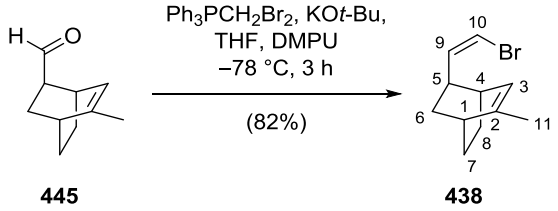
^{1}H NMR (300 MHz, $CDCl_3$): δ = 9.42 (d, $^3J_{C9\text{-}H,C2\text{-}H}$ = 1.6 Hz, 1H, C9-H), 5.72 – 5.66 (m, 1H, C6-H), 2.90 – 2.82 (m, 1H, C1-H), 2.54 – 2.46 (m, 1H, C2-H), 2.45 – 2.39 (m, 1H, C4-H), 1.76 (d, $^4J_{C10\text{-}H,C6\text{-}H}$ = 1.7 Hz, 3H, C10-H), 1.74 – 1.45 (m, 4H, C3-H, C7-H_{syn}, C8-H_{syn}), 1.41 – 1.22 (m, 2H, C7-H_{anti}, C8-H_{anti}) ppm.

^{13}C NMR (75 MHz, $CDCl_3$): δ = 204.6 (C9), 145.1 (C5), 123.1 (C6), 52.0 (C2), 35.1 (C4), 31.7 (C1), 26.7 (C3), 26.4 (C7), 24.8 (C8), 20.3 (C10) ppm.

IR (ATR): $\tilde{\nu}$ = 3429 (br w), 2935 (m), 2870 (w), 1711 (vs), 1452 (w), 1375 (w), 1353 (w), 1176 (m), 1095 (m), 1046 (m), 995 (m), 967 (m), 923 (w), 725 (vw) cm^{-1}.

HRMS (EI): m/z for $C_{10}H_{14}O^+$ $[M]^+$: calcd.: 150.1039
found: 150.1037.

5-(*endo*-(*Z*)-2-Bromoalkenyl)-2-methylbicyclo[2.2.2]oct-2-ene (438)



445 **438**

To a solution of (bromomethyl)triphenylphosphonium bromide (9.59 g, 22.0 mmol, 1.10 eq.) in THF (91.0 mL) at −78 °C was added KO*t*-Bu (2.47 g, 22.0 mmol, 1.10 eq.). The resulting yellow reaction mixture was stirred at −78 °C for 30 min, after which time DMPU (11.3 mL, 12.0 g, 94.0 mmol, 4.70 eq.) and aldehyde **445** (3.00 g, 20.0 mmol, 1.00 eq.) were added successively. The mixture was stirred for an additional 3 h at −78 °C and was then diluted with hexanes (300 mL) and filtered over celite. The residue was washed with hexanes (300 mL) and the combined filtrates were concentrated *in vacuo*. Purification of the residue by flash column chromatography (5 x 20 cm, silica, hexanes : EtOAc = 1000 : 1, 100 mL, #6–8) afforded alkenyl bromide **438** (3.74 g, 82%) as a colorless oil.

$C_{11}H_{15}Br$ $M_r = 227.14\ g{\cdot}mol^{-1}$.

TLC $R_f = 0.73$ (hexanes).

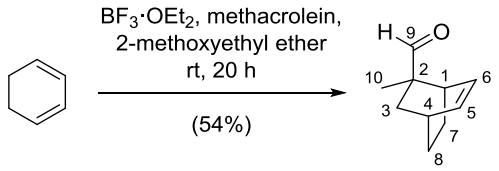
^{1}H NMR (300 MHz, $CDCl_3$): δ = 5.95 (dd, $^3J_{C10\text{-}H,C9\text{-}H} = 6.8$ Hz, $^4J_{C10\text{-}H,C5\text{-}H} = 0.8$ Hz, 1H, C10-H), 5.81 (dd, $^3J_{C9\text{-}H,C5\text{-}H} = 8.9$ Hz, $^3J_{C9\text{-}H,C10\text{-}H} = 6.8$ Hz, 1H, C9-H), 5.78 – 5.73 (m, 1H, C3-H), 2.87 – 2.75 (m, 1H, C5-H), 2.42 – 2.35 (m, 1H, C4-H), 2.35 – 2.30 (m, 1H, C1-H), 1.91 (ddd, $^2J_{C6\text{-}Hexo,C6\text{-}Hendo} = 12.5$ Hz, $^3J_{C6\text{-}Hexo,C5\text{-}H} = 9.6$ Hz, $^3J_{C6\text{-}Hexo,C1\text{-}H} = 2.7$ Hz, 1H, C6-H_{exo}), 1.80 (d, $^4J_{C11\text{-}H,C3\text{-}H} = 1.7$ Hz, 3H, C11-H), 1.65 – 1.54 (m, 1H, C8-H_{anti}), 1.53 – 1.43 (m, 1H, C7-H_{anti}), 1.32 – 1.18 (m, 2H, C7-H_{syn}, C8-H_{syn}), 0.98 (dddd, $^2J_{C6\text{-}Hendo,C6\text{-}Hexo} = 12.5$ Hz, $^3J_{C6\text{-}Hendo,C5\text{-}H} = 5.0$ Hz, $^3J_{C6\text{-}Hendo,C1\text{-}H} = 2.8$ Hz, $^4J_{C6\text{-}Hendo,C7\text{-}Hsyn} = 2.8$ Hz, 1H, C6-H_{endo}) ppm.

^{13}C NMR (75 MHz, $CDCl_3$) δ = 144.2 (C2), 142.0 (C9), 124.2 (C3), 104.5 (C10), 39.6 (C5), 35.3 (C1), 34.9 (C4), 33.4 (C6), 26.7 (C8), 24.2 (C7), 20.4 (C11) ppm.

IR (ATR): $\tilde{\nu}$ = 3077 (vw), 3029 (vw), 2930 (s), 2861 (m), 1719 (vw), 1686 (vw), 1650 (vw), 1616 (vw), 1464 (vw), 1443 (w), 1376 (vw), 1349 (vw), 1339 (vw), 1322 (w), 1310 (vw), 1290 (w), 1277 (s), 1242 (vw), 1197 (vw), 1177 (vw), 1161 (vw), 1145 (vw), 1094 (vw), 1041 (vw), 1021 (vw), 981 (w), 965 (vw), 940 (w), 912 (w), 854 (w), 808 (s), 799 (m), 707 (vs), 663 (m) cm^{-1}.

HRMS (EI): m/z for $C_{11}H_{15}Br^+$ $[M]^+$: calcd.: 226.0352
found: 226.0345.

2-Methylbicyclo[2.2.2]oct-5-en-2-*endo*-carbaldehyde (446)



243 **446**

To a solution of cyclohexadiene **243** (3.73 mL, 3.21 g, 40.0 mmol, 2.00 eq.) in 2-methoxyethyl ether (20.0 mL) at room temperature was added successively methacrolein (1.66 mL, 1.40 g, 20.0 mmol, 1.00 eq.) and $BF_3 \cdot Et_2O$ (0.370 mL, 0.426 g, 3.00 mmol, 0.150 eq.). The reaction mixture was stirred at room temperature for 20 h and was then quenched by addition of K_2HPO_4 (522 mg, 3.00 mmol, 0.150 eq.). The mixture was diluted with H_2O (25 mL) and the aqueous layer was extracted with Et_2O (3 x 30 mL). The combined organic layer was washed with H_2O (3 x 25 mL), dried (Na_2SO_4) and concentrated *in vacuo*. Purification of the residue by flash column chromatography (4 x 20 cm, silica, *n*-pentane : Et_2O = 97 : 3, 20 mL, #21–30) afforded bicycloaldehyde **446** (1.64 g, 54%) as a colorless oil.

$C_{10}H_{14}O$ M_r = 150.22 g·mol^{-1}.

TLC R_f = 0.53 (hexanes : EtOAc = 9 : 1).

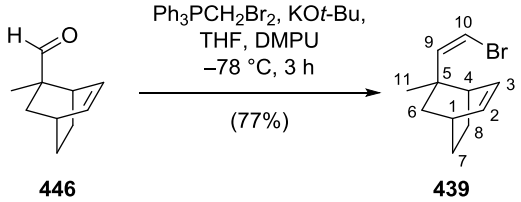
^{1}H NMR (400 MHz, $CDCl_3$): δ = 9.30 (s, 1H, C9-H), 6.26 – 6.19 (m, 2H, C5-H, C6-H), 2.62 – 2.55 (m, 1H, C4-H), 2.49 – 2.43 (m, 1H, C1-H), 2.03 – 1.96 (m, 1H, C3-H_{exo}), 1.92 – 1.84 (m, 1H, C7-H_{syn}), 1.56 – 1.47 (m, 1H, C8-H_{syn}), 1.30 – 1.10 (m, 6H, C3-H_{endo}, C7-H_{anti}, C8-H_{anti}, C10-H) ppm.

^{13}C NMR (100 MHz, $CDCl_3$): δ = 205.7 (C9), 135.2 (C5), 133.6 (C6), 50.0 (C2), 36.1 (C1), 35.6 (C3), 30.6 (C4), 25.2 (C8), 21.3 (C10), 20.3 (C7) ppm.

IR (ATR): $\tilde{\nu}$ = 3045 (vw), 2943 (m), 2866 (w), 2805 (vw), 2692 (vw), 1721 (vs), 1615 (vw), 1472 (vw), 1449 (w), 1368 (w), 1310 (vw), 1229 (vw), 1172 (vw), 1104 (vw), 1074 (w), 1058 (w), 1041 (w), 999 (vw), 980 (vw), 952 (vw), 900 (m), 841 (vw), 812 (w), 732 (vw), 693 (vs), 668 (w) cm^{-1}.

HRMS (EI): m/z for $C_{10}H_{14}O^+$ $[M]^+$: calcd.: 150.1039
found: 150.1048.

5-(*endo*-(*Z*)-2-Bromoalkenyl)-5-methylbicyclo[2.2.2]oct-2-ene (439)



446 **439**

To a solution of (bromomethyl)triphenylphosphonium bromide (3.48 g, 7.99 mmol, 1.10 eq.) in THF (33.0 mL) at −78 °C was added KO*t*-Bu (0.896 g, 7.99 mmol, 1.10 eq.). The resulting yellow reaction mixture was stirred at −78 °C for 15 min, after which time DMPU (4.11 mL, 4.37 g, 34.1 mmol, 4.70 eq.) and aldehyde **446** (1.09 g, 7.26 mmol, 1.00 eq.) were added successively. The mixture was stirred for an additional 3 h at −78 °C and was then diluted with hexanes (200 mL) and filtered over celite. The residue was washed with hexanes (200 mL) and the combined filtrates were concentrated *in vacuo*. Purification of the residue by flash column chromatography (4 x 26 cm, silica, hexanes : EtOAc = 100 : 1, 20 mL, #14–18) afforded alkenyl bromide **439** (1.27 g, 77%) as a colorless oil.

$C_{11}H_{15}Br$ M_r = 227.14 g·mol^{-1}.

TLC R_f = 0.85 (hexanes : EtOAc = 9 : 1).

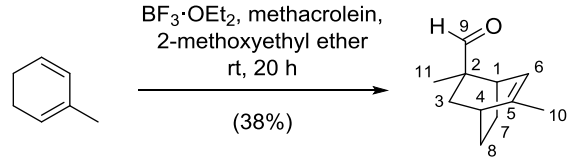
^{1}H NMR (300 MHz, $CDCl_3$): δ = 6.37 – 6.24 (m, 2H, C2-H, C3-H), 6.20 (d, $^3J_{C9\text{-}H,C10\text{-}H}$ = 7.6 Hz, 1H, C9-H), 5.92 (d, $^3J_{C10\text{-}H,C9\text{-}H}$ = 7.6 Hz, 1H, C10-H), 2.57 – 2.45 (m, 2H, C1-H, C4-H), 1.98 – 1.84 (m, 2H, C6-H_{endo}, C8-H_{anti}), 1.57 (dd, $^2J_{C6\text{-}Hexo,C6\text{-}Hendo}$ = 12.9 Hz, $^3J_{C6\text{-}Hexo,C1\text{-}H}$ = 2.4 Hz, 1H, C6-H_{exo}), 1.53 – 1.40 (m, 1H, C7-H_{anti}), 1.37 (s, 3H, C11-H), 1.30 – 1.05 (m, 2H, C7-H_{syn}, C8-H_{syn}) ppm.

^{13}C NMR (75 MHz, $CDCl_3$): δ = 146.9 (C9), 135.0 (C2, C3), 103.8 (C10), 45.1 (C6), 41.1 (C4), 40.2 (C5), 31.5 (C1), 25.5 (C11), 24.4 (C7), 20.9 (C8) ppm.

IR (ATR): $\tilde{\nu}$ = 3043 (vw), 2940 (w), 2922 (w), 2862 (w), 1608 (w), 1472 (vw), 1443 (w), 1374 (vw), 1367 (w), 1329 (vw), 1312 (m), 1286 (vw), 1270 (vw), 1256 (vw), 1204 (vw), 1169 (vw), 1139 (vw), 1106 (vw), 1095 (vw), 1041 (vw), 982 (vw), 938 (vw), 911 (m), 898 (vw), 865 (vw), 848 (vw), 811 (w), 746 (w), 702 (vs), 692 (vs), 671 (w), 641 (w), 615 (w), 566 (m) cm^{-1}.

HRMS (EI): m/z for $C_{11}H_{15}^+$ $[M–Br]^+$: calcd.: 147.1168
found: 147.1159.

2,5-Dimethylbicyclo[2.2.2]oct-5-ene-2-*endo*-carbaldehyde (447)



444 **447**

To a solution of methylcyclohexadiene **444** (2.27 mL, 1.88 g, 20.0 mmol, 1.00 eq.) in 2-methoxyethyl ether (20.0 mL) at room temperature was added successively methacrolein (2.48 mL, 2.10 g, 30.0 mmol, 1.50 eq.) and $BF_3 \cdot Et_2O$ (0.370 mL, 0.426 g, 3.00 mmol, 0.300 eq.). The reaction mixture was stirred at room temperature for 20 h. The mixture was diluted with H_2O (25 mL) and the aqueous layer was extracted with Et_2O (3 x 25 mL). The combined organic layer was washed with H_2O (3 x 25 mL), dried (Na_2SO_4) and concentrated *in vacuo*. Purification of the residue by flash column chromatography (5 x 20 cm, silica, *n*-pentane : Et_2O = 95 : 5, 100 mL, #10–14) afforded bicycloaldehyde **447** (1.24 g, 38%) as a colorless oil.

$C_{11}H_{16}O$ M_r = 164.24 g·mol^{-1}.

TLC R_f = 0.44 (*n*-pentane : Et_2O = 95 : 5).

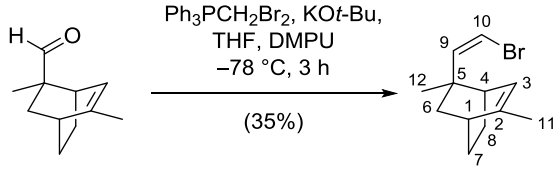
^{1}H NMR (600 MHz, $CDCl_3$): δ = 9.30 (s, 1H, C9-H), 5.82 – 5.79 (m, 1H, C6-H), 2.40 – 2.37 (m, 1H, C1-H), 2.37 – 2.34 (m, 1H, C4-H), 2.02 (ddd, $^2J_{C3\text{-}Hendo,C3\text{-}Hexo}$ = 13.0 Hz, $^3J_{C3\text{-}Hendo,C4\text{-}H}$ = 3.2 Hz, $^4J_{C3\text{-}Hendo,C8\text{-}Hanti}$ = 3.2 Hz, 1H, C3-H_{endo}), 1.87 (dddd, $^2J_{C7\text{-}Hsyn,C7\text{-}Hanti}$ = 12.8 Hz, $^3J_{C7\text{-}Hsyn,C8\text{-}Hsyn}$ = 9.6 Hz, $^3J_{C7\text{-}Hsyn,C1\text{-}H}$ = 3.1 Hz, $^3J_{C7\text{-}Hsyn,C8\text{-}Hanti}$ = 3.1 Hz, 1H, C7-H_{syn}), 1.73 (d, $^4J_{C10\text{-}H,C6\text{-}H}$ = 1.7 Hz, 3H, C10-H), 1.50 (dddd, $^2J_{C8\text{-}Hsyn,C8\text{-}Hanti}$ = 12.0 Hz, $^3J_{C8\text{-}Hsyn,C7\text{-}Hsyn}$ = 9.6 Hz, $^3J_{C8\text{-}Hsyn,C7\text{-}Hanti}$ = 4.7 Hz, $^3J_{C8\text{-}Hsyn,C4\text{-}H}$ = 2.4 Hz, 1H, C8-H_{syn}), 1.26 (ddddd, $^2J_{C8\text{-}Hanti,C8\text{-}Hsyn}$ = 12.0 Hz, $^3J_{C8\text{-}Hanti,C7\text{-}Hanti}$ = 9.9 Hz, $^3J_{C8\text{-}Hanti,C4\text{-}H}$ = 3.2 Hz, $^4J_{C8\text{-}Hanti,C3\text{-}Hendo}$ = 3.2 Hz, $^3J_{C8\text{-}Hanti,C7\text{-}Hsyn}$ = 3.1 Hz, 1H, C8-H_{anti}), 1.21 – 1.14 (dddd, $^2J_{C7\text{-}Hanti,C7\text{-}Hsyn}$ = 12.8 Hz, $^3J_{C7\text{-}Hanti,C8\text{-}Hanti}$ = 9.9 Hz, $^3J_{C7\text{-}Hanti,C8\text{-}Hsyn}$ = 4.8 Hz, $^3J_{C7\text{-}Hanti,C1\text{-}H}$ = 3.2 Hz, 1H, C7-H_{anti}), 1.11 (s, 3H, C11-H), 1.10 (dd, $^2J_{C3\text{-}Hexo,C3\text{-}Hendo}$ = 13.0 Hz, $^3J_{C3\text{-}Hexo,C4\text{-}H}$ = 2.4 Hz, 1H, C3-H_{exo}) ppm.

^{13}C NMR (150 MHz, $CDCl_3$): δ = 206.0 (C9), 144.1 (C5), 125.6 (C6), 50.6 (C2), 36.8 (C1), 36.3 (C4), 35.1 (C3), 25.0 (C8), 21.3 (C11), 21.0 (C7), 20.2 (C10) ppm.

IR (ATR): $\tilde{\nu}$ = 3469 (br vw), 2930 (vs), 2869 (s), 1713 (vs), 1447 (m), 1377 (m), 1162 (m), 1103 (vs), 1067 (m), 990 (s), 756 (w), 667 (vw) cm^{-1}.

HRMS (EI): m/z for $C_{11}H_{16}O^+$ $[M]^+$: calcd.: 164.1196
found: 164.1204.

5-(*endo*-(*Z*)-2-Bromoalkenyl)-2,5-dimethylbicyclo[2.2.2]oct-2-ene (440)



447 **440**

To a solution of (bromomethyl)triphenylphosphonium bromide (3.60 g, 8.25 mmol, 1.10 eq.) in THF (34.0 mL) at −78 °C was added KO*t*-Bu (0.926 g, 8.25 mmol, 1.10 eq.). The resulting yellow reaction mixture was stirred at −78 °C for 30 min, after which time DMPU (4.25 mL, 4.52 g, 35.3 mmol, 4.70 eq.) and aldehyde **447** (1.23 g, 7.50 mmol, 1.00 eq.) were added successively. The mixture was stirred for an additional 3 h at −78 °C and was then diluted with hexanes (600 mL) and filtered over celite. The residue was washed with hexanes (600 mL) and the combined filtrates were concentrated *in vacuo*. Purification of the residue by flash column chromatography (5 x 21 cm, silica, hexanes : EtOAc = 1000 : 1, 100 mL, #7-8) afforded alkenyl bromide **440** (620 mg, 35%) as a colorless oil.

$C_{12}H_{17}Br$ M_r = 240.05 g·mol^{-1}.

TLC R_f = 0.91 (hexanes : EtOAc = 9 : 1).

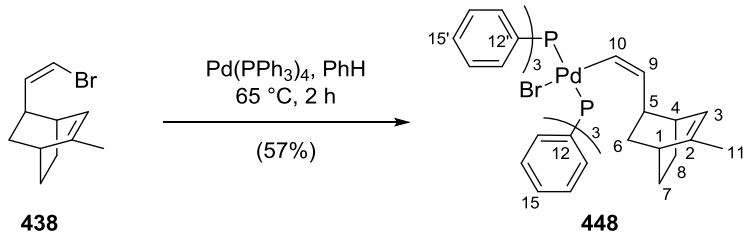
^{1}H NMR (300 MHz, $CDCl_3$): δ = 6.20 (d, $^3J_{C9\text{-}H,C10\text{-}H}$ = 7.6 Hz, 1H, C9-H), 5.94 – 5.89 (m, 1H, C3-H), 5.90 (d, $^3J_{C10\text{-}H,C9\text{-}H}$ = 7.6 Hz, 1H, C10-H), 2.39 – 2.33 (ddd, $^3J_{C4\text{-}H,C3\text{-}H}$ = 6.2 Hz, $^3J_{C4\text{-}H,C8\text{-}Hsyn}$ = 2.9 Hz, $^3J_{C4\text{-}H,C8\text{-}Hanti}$ = 2.9 Hz, 1H, C4-H), 2.33 – 2.26 (m, 1H, C1-H), 1.97 – 1.81 (m, 2H, C6-H_{endo}, C8-H_{anti}), 1.76 (d, $^4J_{C11\text{-}H,C3\text{-}H}$ = 1.7 Hz, 3H, C11-H), 1.55 (dd, $^2J_{C3\text{-}Hexo,C3\text{-}Hendo}$ = 12.9 Hz, $^2J_{C3\text{-}Hexo,C1\text{-}H}$ = 2.4 Hz, 1H, C3-H_{exo}), 1.44 (dddd, $^2J_{C7\text{-}Hanti,C7\text{-}Hsyn}$ = 11.7 Hz, $^3J_{C7\text{-}Hanti,C8\text{-}Hanti}$ = 9.4 Hz, $^3J_{C7\text{-}Hanti,C8\text{-}Hsyn}$ = 5.1 Hz, $^3J_{C7\text{-}Hanti,C4\text{-}H}$ = 2.9 Hz, 1H, C7-H_{anti}), 1.35 (s, 3H, C12-H), 1.24 (ddddd, $^2J_{C7\text{-}Hsyn,C7\text{-}Hanti}$ = 11.7 Hz, $^3J_{C7\text{-}Hsyn,C8\text{-}Hsyn}$ = 9.4 Hz, $^3J_{C7\text{-}Hsyn,C8\text{-}Hanti}$ = 3.2 Hz, $^3J_{C7\text{-}Hsyn,C1\text{-}H}$ = 3.2 Hz, $^4J_{C7\text{-}Hsyn,C6\text{-}Hendo}$ = 3.2 Hz, 1H, C7-H_{syn}), 1.16 – 1.03 (m, 1H, C8-H_{syn}) ppm.

^{13}C NMR (75 MHz, $CDCl_3$): δ = 147.2 (C9), 143.5 (C2), 127.0 (C3), 103.6 (C10), 44.5 (C6), 41.8 (C4), 40.7 (C5), 37.1 (C1), 25.6 (C12), 23.9 (C7), 21.8 (C8), 20.4 (C11) ppm.

IR (ATR): $\tilde{\nu}$ = 3074 (vw), 3029 (vw), 2919 (m), 2861 (w), 1652 (vw), 1609 (w), 1473 (vw), 1443 (m), 1373 (w), 1356 (vw), 1313 (m), 1287 (vw), 1257 (vw), 1205 (vw), 1158 (vw), 1138 (vw), 1113 (w), 1096 (vw), 1045 (vw), 973 (vw), 915 (m), 852 (vw), 820 (w), 800 (w), 742 (m), 692 (vs), 656 (vw) cm^{-1}.

HRMS (EI): m/z for $C_{12}H_{17}Br^+$ $[M]^+$: calcd.: 240.0508
found: 240.0515.

(*Z*)-2-(2-Methylbicyclo[2.2.2]oct-2-en-5-*endo*-yl)alkenylbis(triphenylphosphine)palladium(II) bromide (448)



438 **448**

To a solution of $Pd(PPh_3)_4$ (994 mg, 0.860 mmol, 1.00 eq.) in benzene (6.00 mL) was added (*Z*)-alkenyl bromide **438** (195 mg, 0.860 mmol, 1.00 eq.) by syringe. The yellow reaction mixture was heated to 65 °C for 2 h. The mixture was allowed to cool to room temperature and Et_2O (50 mL) was added, precipitating a white solid. The precipitate was filtered off and the filtrate was allowed to stand. Upon slow evaporation of the solvent palladium complex **448** (290 mg, 57%) crystallized in the form of yellow platelets. Crystals suitable for single crystal X-ray diffraction could be obtained from this mixture. For NMR analysis the reaction was run in C_6D_6 in a NMR tube resulting in a mixture of starting material and product in the NMR.

$C_{47}H_{45}BrP_2Pd$ M_r = 858.13 g·mol^{-1}.

mp 123 °C (dec.).

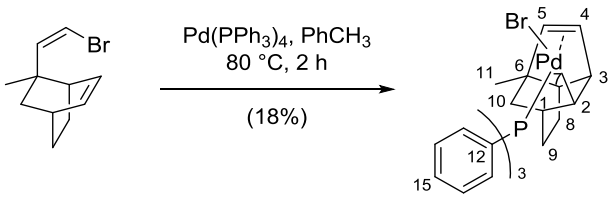
^{1}H NMR (400 MHz, C_6D_6): δ = 7.99 – 7.92 (m, 12H, C13-H), 7.44 (m, 18H, C14-H, C15-H), 5.75 (td, $^3J_{C10\text{-}H,P}$ = 10.4 Hz, $^3J_{C10\text{-}H,C9\text{-}H}$ = 7.2 Hz, 1H, C10-H), 5.54 (dq, $^3J_{C3\text{-}H,C4\text{-}H}$ = 6.7 Hz, $^4J_{C3\text{-}H,C11\text{-}H}$ = 1.7 Hz, 1H, C3-H), 4.95 (ddt, $^3J_{C9\text{-}H,C5\text{-}H}$ = 9.4 Hz, $^3J_{C9\text{-}H,C10\text{-}H}$ = 7.3 Hz, $^4J_{C9\text{-}H,P}$ = 4.7 Hz, 1H, C9-H), 3.07 (dddd, $^3J_{C5\text{-}H,C9\text{-}H}$ = 9.4, $^3J_{C5\text{-}H,C6\text{-}Hexo}$ = 9.3 Hz, $^3J_{C5\text{-}H,C6\text{-}Hendo}$ = 4.8 Hz, $^3J_{C5\text{-}H,C4\text{-}H}$ = 2.0 Hz, 1H, C5-H), 2.14 – 2.06 (m, 1H, C1-H*), 2.02 – 1.94 (m, 1H, C4-H*), 1.88 – 1.78 (m, 1H, C7-H_A**), 1.60 (d, $^4J_{C11\text{-}H,C3\text{-}H}$ = 1.7 Hz, 3H, C11-H), 1.57 – 1.50 (m, 1H, C8-H_A**), 1.37 (ddd, $^2J_{C6\text{-}Hexo,C6\text{-}Hendo}$ = 12.4 Hz, $^3J_{C6\text{-}Hexo,C5\text{-}H}$ = 9.3 Hz, $^3J_{C6\text{-}Hexo,C1\text{-}H}$ = 2.7 Hz, 1H, C6-H_{exo}), 1.32 – 1.24 (m, 2H, C7-H_B, C8-H_B), 0.64 (dddd, $^2J_{C6\text{-}Hendo,C6\text{-}Hexo}$ = 12.4 Hz, $^3J_{C6\text{-}Hendo,C5\text{-}H}$ = 4.8 Hz, $^3J_{C6\text{-}Hendo,C1\text{-}H}$ = 2.6 Hz, $^4J_{C6\text{-}Hendo,C7\text{-}Hsyn}$ = 2.6 Hz, 1H, C6-H_{endo}) ppm.

^{13}C NMR (100 MHz, C_6D_6): δ = 144.2 (C10), 142.7 (C2), 137.7 (C9), 135.9 (C13), 134.3 (C14*), 134.1 (C15*), 132.5 (d, $^1J_{C12,P}$ = 44.0 Hz, C12), 125.0 (C3), 47.0 (C5), 36.2 (C1**), 36.1 (C4**), 34.7 (C6), 27.8 (C7***), 24.8 (C8***), 20.4 (C11) ppm.

IR (ATR): $\tilde{\nu}$ = 3049 (vw), 2914 (vw), 2851 (vw), 1585 (vw), 1570 (vw), 1478 (w), 1434 (m), 1329 (vw), 1309 (w), 1287 (vw), 1262 (w), 1225 (vw), 1183 (w), 1117 (vw), 1094 (m), 1071 (vw), 1027 (w), 998 (w), 910 (vw), 864 (vw), 807 (vw), 751 (w), 741 (s), 703 (s), 689 (vs), 677 (vs) cm^{-1}.

HRMS (ESI+): m/z for $C_{29}H_{30}PPd^+$ [M–PPh_3–Br]$^+$: calcd.: 515.1114
found: 515.1117.

6-Methyltricyclo[4.3.1.0^{3,7}]dec-4-ene-2-yltriphenylphosphinepalladium(II) bromide (450)



439 **450**

To a solution of $Pd(PPh_3)_4$ (497 mg, 0.430 mmol, 1.00 eq.) in toluene (3.00 mL) was added (*Z*)-alkenyl bromide **439** (97.7 mg, 0.430 mmol, 1.00 eq.) by syringe. The yellow reaction mixture was heated to 80 °C for 2 h. The mixture was allowed to cool to room temperature and Et_2O (50 mL) was added, precipitating a white solid. The precipitate was filtered off and the filtrate was allowed to stand. Upon slow evaporation of the solvent palladium complex **450** (45 mg, 18%) crystallized in the form of yellow platelets. Crystals suitable for single crystal X-ray diffraction could be obtained from this mixture.

$C_{29}H_{30}BrPPd$ M_r = 595.85 g·mol^{-1}.

mp 158 °C (dec.).

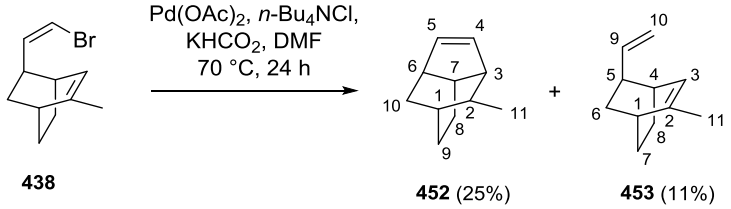
^{1}H NMR (600 MHz, $CDCl_3$): δ = 7.75 – 7.69 (m, 6H, C13-H), 7.46 – 7.38 (m, 9H, C14-H, C15-H), 6.61 – 6.56 (m, 1H, C5-H), 6.15 – 6.12 (m, 1H, C4-H), 3.23 – 3.17 (m, 1H, C3-H), 3.04 (dd, $^3J_{C10\text{-}Ha,C10\text{-}Hb}$ = 13.0 Hz, $^3J_{C10\text{-}Ha,C1\text{-}H}$ = 4.1 Hz, 1H, C10-H_A), 1.83 – 1.78 (m, 1H, C7-H), 1.61 – 1.52 (m, 1H, C8-H_A), 1.47 – 1.32 (m, 3H, C8-H_B, C9-H_A, C10-H_B), 1.27 – 1.21 (m, 1H, C1-H), 1.16 (s, 3H, C11-H), 0.99 – 0.89 (m, 2H, C2-H, C9-H_B) ppm.

^{13}C NMR (150 MHz, $CDCl_3$): δ = 136.9 (d, $^2J_{C5,P}$ = 10.0 Hz, C5), 134.7 (d, $^2J_{C13,P}$ = 12.3 Hz, C13), 131.0 (d, $^1J_{C12,P}$ = 43.9 Hz, C12), 130.7 (d, $^4J_{C15,P}$ = 2.4 Hz, C15), 128.5 (d, $^3J_{C14,P}$ = 10.4 Hz, C14), 85.1 (d, $^2J_{C4,P}$ = 13.3 Hz, C4), 52.6 (s, C7), 50.2 (s, C3), 45.5 (d, $^3J_{C6,P}$ = 2.4 Hz, C6), 41.4 (s, C10), 32.6 (s, C1), 30.3 (d, $^4J_{C9,P}$ = 5.1 Hz, C9), 26.7 (d, $^2J_{C2,P}$ = 7.4 Hz, C2), 23.4 (s, C11), 16.0 (s, C8) ppm.

IR (ATR): $\tilde{\nu}$ = 3857 (vw), 3754 (vw), 3738 (vw), 3635 (vw), 3060 (vw), 2933 (vw), 2861 (vw), 2361 (vs), 2339 (s), 1734 (vw), 1653 (vw), 1560 (vw), 1540 (vw), 1481 (vw), 1436 (w), 1340 (vw), 1095 (vw), 1027 (vw), 916 (vw), 743 (w), 739 (w), 694 (w), 668 (m) cm^{-1}.

HRMS (ESI+): m/z for $C_{29}H_{30}PPd^+$ $[M–Br]^+$: calcd.: 515.1114
found: 515.1117.

Cyclization of Alkenyl Bromide 438 with Catalytic Amounts of Palladium



438 **452** (25%) **453** (11%)

To a round bottom flask were added $Pd(OAc)_2$ (12.3 mg, 0.055 mmol, 0.025 eq.), *n*-Bu_4NCl (611 mg, 2.20 mmol, 1.00 eq.) and potassium formate (555 mg, 6.60 mmol, 3.00 eq.). The flask was evacuated and refilled with argon three times. The salts were dissolved in degassed DMF (132 mL) and alkenyl bromide **438** (0.500 g, 2.20 mmol, 1.00 eq.) was added. The reaction mixture was transferred to a preheated oil bath and stirred at 70 °C for 24 h. During the reaction the color of the mixture turned from yellow to black. The reaction mixture was allowed to cool to room temperature and was diluted with H_2O (110 mL) and pentane (110 mL) and the resulting mixture was stirred for 15 min at room temperature. The organic layer was separated and the aqueous layer was extracted with *n*-pentane (3 x 110 mL). The combined organic layer was dried (Na_2SO_4) and concentrated *in vacuo* (at room temperature). Purification of the residue by flash column chromatography (3 x 24 cm, silica, *n*-pentane, 20 mL) afforded methylisotwistene **452** (#10, 80 mg, 25%) as a colorless oil and vinyl bicyclooctene **453** (#13–15, 35 mg, 11%) contaminated with isotwistene **452** as a colorless oil.

*2-Methyltricyclo[4.3.1.0^{3,7}]dec-4-ene (**452**)*

$C_{11}H_{16}$ M_r = 148.25 g·mol^{-1}.

TLC R_f = 0.78 (hexanes).

^{1}H NMR (600 MHz, $CDCl_3$): δ = 6.09 (dd, $^3J_{C4\text{-}H,C5\text{-}H}$ = 5.7 Hz, $^3J_{C4\text{-}H,C3\text{-}H}$ = 3.0 Hz, 1H, C4-H), 6.07 (dd, $^3J_{C5\text{-}H,C4\text{-}H}$ = 5.7 Hz, $^3J_{C5\text{-}H,C6\text{-}H}$ = 2.9 Hz, 1H, C5-H), 2.27 – 2.23 (m, 1H, C6-H), 2.08 – 2.04 (m, 1H, C7-H), 1.87 – 1.79 (m, 1H, C9-H_{endo}), 1.79 – 1.74 (m, 3H, C3-H, C8-H), 1.70 – 1.67 (m, 1H, C1-H), 1.67 – 1.62 (m, 1H, C2-H), 1.48 – 1.44 (m, 2H, C10-H), 1.31 – 1.23 (m, 1H, C9-H_{exo}), 0.94 (d, $^3J_{C11\text{-}H,C2\text{-}H}$ = 7.2 Hz, 3H, C11-H) ppm.

^{13}C NMR (150 MHz, $CDCl_3$): δ = 140.5 (C5), 139.6 (C4), 47.2 (C3), 41.0 (C7), 38.5 (C6), 34.6 (C1), 32.6 (C2), 31.6 (C10), 21.1 (C11), 20.7 (C9), 19.2 (C8) ppm.

IR (ATR): $\tilde{\nu}$ = 3403 (w), 2924 (vs), 2864 (s), 1713 (m), 1454 (m), 1404 (w), 1373 (m), 1352 (m), 1266 (w), 1187 (m), 1131 (m), 1104 (s), 1095 (s), 1067 (vs), 1041 (s), 1018 (s), 994 (m), 927 (w), 913 (w), 885 (w), 853 (w), 808 (vw), 753 (s), 666 (w) cm^{-1}.

HRMS (EI): m/z for $C_{11}H_{16}^+$ $[M]^+$: calcd.: 148.1247
found: 148.1243.

*2-Methyl-5-endo-vinylbicyclo[2.2.2]oct-2-ene (**453**)*

$C_{11}H_{16}$ M_r = 148.25 g·mol^{-1}.

TLC R_f = 0.68 (hexanes).

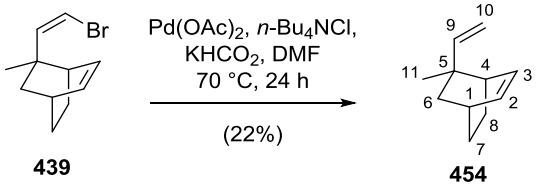
^{1}H NMR (600 MHz, $CDCl_3$): δ = 5.77 – 5.74 (m, 1H, C3-H), 5.56 (ddd, $^3J_{C9\text{-}H,C10\text{-}Hz}$ = 17.2 Hz, $^3J_{C9\text{-}H,C10\text{-}HE}$ = 10.2 Hz, $^3J_{C9\text{-}H,C5\text{-}H}$ = 8.2 Hz, 1H, C9-H), 4.87 (ddd, $^3J_{C10\text{-}Hz,C9\text{-}H}$ = 17.2 Hz, $^3J_{C10\text{-}Hz,C10\text{-}HE}$ = 2.0 Hz, $^4J_{C10\text{-}Hz,C5\text{-}H}$ = 1.1 Hz, 1H, C10-H$_Z$), 4.79 (ddd, $^3J_{C10\text{-}HE,C9\text{-}H}$ = 10.2 Hz, $^3J_{C10\text{-}HE,C10\text{-}Hz}$ = 2.0 Hz, $^3J_{C10\text{-}HE,C5\text{-}H}$ = 0.9 Hz, 1H, C10-H$_E$), 2.37 – 2.34 (m, 1H, C4-H), 2.34 – 2.31 (m, 1H, C5-H), 2.31 – 2.28 (m, 1H, C1-H), 1.79 (d, $^4J_{C11\text{-}H,C3\text{-}H}$ = 1.8 Hz, 3H, C11-H), 1.78 – 1.74 (m, 1H, C6-H$_{exo}$), 1.57 – 1.51 (m, 1H, C8-H$_{anti}$), 1.48 – 1.43 (m, 1H, C7-H$_{anti}$), 1.27 – 1.21 (m, 2H, C7-H$_{syn}$, C8-H$_{syn}$), 1.08 – 1.02 (m, 1H, C6-H$_{endo}$) ppm.

^{13}C NMR (150 MHz, $CDCl_3$): δ = 145.9 (C9), 143.3 (C2), 124.3 (C3), 111.5 (C10), 43.4 (C5), 36.3 (C4), 35.6 (C1), 33.5 (C6), 27.2 (C8), 24.3 (C7), 20.3 (C11) ppm.

IR (ATR): $\tilde{\nu}$ = 3418 (vw), 3028 (vw), 2926 (vs), 2862 (vs), 1710 (s), 1652 (vw), 1453 (m), 1375 (w), 1356 (w), 1335 (w), 1168 (m), 1102 (w), 1067 (w), 1041 (w), 995 (w), 967 (w), 913 (w), 876 (w), 852 (w), 805 (w), 733 (w) cm^{-1}.

HRMS (EI): m/z for $C_{11}H_{16}^+$ $[M]^+$: calcd.: 148.1247
found: 148.1253.

5-Methyl-5-*endo*-vinylbicyclo[2.2.2]oct-2-ene (454)



439 **454**

To a round bottom flask were added $Pd(OAc)_2$ (2.8 mg, 0.013 mmol, 0.025 eq.), *n*-Bu_4NCl (139 mg, 0.500 mmol, 1.00 eq.) and potassium formate (126 mg, 1.50 mmol, 3.00 eq.). The flask was evacuated and refilled with argon three times. The salts were dissolved in degassed DMF (30.0 mL) and alkenyl bromide **439** (114 mg, 0.500 mmol, 1.00 eq.) was added. The reaction mixture was transferred to a preheated oil bath and stirred at 70 °C for 24 h. During the reaction the color of the mixture turned from yellow to black. The reaction mixture was allowed to cool to room temperature and was diluted with H_2O (30 mL) and pentane (30 mL) and the resulting mixture was stirred for 15 min at room temperature. The organic layer was separated and the aqueous layer was extracted with *n*-pentane (3 x 25 mL). The combined organic layer was dried (Na_2SO_4) and concentrated *in vacuo* (at room temperature). Purification of the residue by flash column chromatography (2 x 10 cm, silica, *n*-pentane, 8 mL, #7–9) afforded vinyl bicyclooctene **454** (16 mg, 22%) as a colorless oil.

$C_{11}H_{16}$ M_r = 148.25 g·mol^{-1}.

TLC R_f = 0.74 (hexanes).

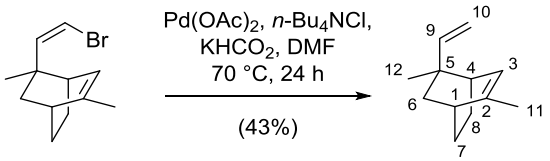
^{1}H NMR (400 MHz, $CDCl_3$): δ = 6.28 (ddd, $^3J_{C3\text{-}H,C2\text{-}H}$ = 8.0 Hz, $^3J_{C3\text{-}H,C4\text{-}H}$ = 6.5 Hz, $^4J_{C3\text{-}H,C1\text{-}H}$ = 1.3 Hz, 1H, C3-H), 6.17 (ddd, $^3J_{C2\text{-}H,C3\text{-}H}$ = 8.0 Hz, $^3J_{C2\text{-}H,C1\text{-}H}$ = 6.0 Hz, $^4J_{C2\text{-}H,C4\text{-}H}$ = 1.2 Hz, 1H, C2-H), 5.77 (dd, $^3J_{C9\text{-}H,C10\text{-}Hz}$ = 17.5 Hz, $^3J_{C9\text{-}H,C10\text{-}He}$ = 10.8 Hz, 1H, C9-H), 4.79 (dd, $^3J_{C10\text{-}Hz,C9\text{-}H}$ = 17.5 Hz, $^2J_{C10\text{-}Hz,C10\text{-}He}$ = 1.4 Hz, 1H, C10-H$_Z$), 4.78 (dd, $^3J_{C10\text{-}He,C9\text{-}H}$ = 10.7 Hz, $^2J_{C10\text{-}He,C10\text{-}Hz}$ = 1.4 Hz, 1H, C10-H$_E$), 2.51 (dddddd, $^3J_{C1\text{-}H,C2\text{-}H}$ = 6.0 Hz, $^3J_{C1\text{-}H,C6\text{-}Hendo}$ = 3.5 Hz, $^3J_{C1\text{-}H,C7\text{-}Hsyn}$ = 3.5 Hz, $^3J_{C1\text{-}H,C6\text{-}Hexo}$ = 2.2 Hz, $^3J_{C1\text{-}H,C7\text{-}Hanti}$ = 2.2 Hz, $^4J_{C1\text{-}H,C3\text{-}H}$ = 1.3 Hz, 1H, C1-H), 2.17 (dddd, $^3J_{C4\text{-}H,C3\text{-}H}$ = 6.5 Hz, $^3J_{C4\text{-}H,C8\text{-}Hsyn}$ = 2.8 Hz, $^3J_{C4\text{-}H,C8\text{-}Hanti}$ = 2.8 Hz, $^3J_{C4\text{-}H,C2\text{-}H}$ = 1.2 Hz, 1H, C4-H), 1.91 (dddd, $^2J_{C8\text{-}Hanti,C8\text{-}Hsyn}$ = 12.7 Hz, $^3J_{C8\text{-}Hanti,C7\text{-}Hanti}$ = 9.7 Hz, $^3J_{C8\text{-}Hanti,C7\text{-}Hsyn}$ = 3.0 Hz, $^3J_{C8\text{-}Hanti,C4\text{-}H}$ = 2.8 Hz, 1H, C8-H$_{anti}$), 1.52 – 1.43 (m, 2H, C6-H$_A$, C7-H$_A$), 1.31 – 1.20 (m, 2H, C6-H$_B$, C7-H$_B$), 1.15 (s, 3H, C11-H), 1.16 – 1.04 (m, 1H, C8-H$_{syn}$) ppm.

^{13}C NMR (100 MHz, $CDCl_3$): δ = 150.9 (C9), 135.7 (C2), 132.4 (C3), 108.9 (C10), 41.0 (C6), 40.4 (C4), 39.6 (C5), 31.1 (C1), 27.1 (C11), 24.2 (C7), 21.8 (C8) ppm.

IR (ATR): $\tilde{\nu}$ = 3080 (vw), 3044 (vw), 2926 (s), 2862 (m), 1817 (vw), 1634 (w), 1615 (vw), 1474 (vw), 1448 (w), 1412 (vw), 1366 (w), 1349 (vw), 1309 (vw), 1230 (vw), 1169 (vw), 1150 (vw), 1127 (vw), 1097 (vw), 1045 (vw), 1005 (w), 933 (vw), 904 (vs), 886 (m), 849 (vw), 816 (w), 810 (w), 731 (w), 716 (vs), 689 (vs) cm^{-1}.

HRMS (EI): m/z for $C_{11}H_{16}^+$ $[M]^+$: calcd.: 148.1247
found: 148.1240.

2,5-Dimethyl-5-*endo*-vinylbicyclo[2.2.2]oct-2-ene (455)



440 **455**

To a round bottom flask were added $Pd(OAc)_2$ (2.8 mg, 0.013 mmol. 0.025 eq.), *n*-Bu_4NCl (139 mg, 0.500 mmol, 1.00 eq.) and potassium formate (126 mg, 1.50 mmol, 3.00 eq.). The flask was evacuated and refilled with argon three times. The salts were dissolved in degassed DMF (30.0 mL) and alkenyl bromide **440** (121 mg, 0.500 mmol, 1.00 eq.) was added. The reaction mixture was transferred to a preheated oil bath and stirred at 70 °C for 24 h. During the reaction the color of the mixture turned from yellow to black. The reaction mixture was allowed to cool to room temperature and was diluted with H_2O (30 mL) and pentane (30 mL) and the resulting mixture was stirred for 15 min at room temperature. The organic layer was separated and the aqueous layer was extracted with *n*-pentane (3 x

25 mL). The combined organic layer was dried (Na_2SO_4) and concentrated *in vacuo* (at room temperature). Purification of the residue by flash column chromatography (2 x 15 cm, silica, *n*-pentane, 8 mL, #8–9) afforded vinyl bicyclooctene **455** (35 mg, 43%) as a colorless oil.

$C_{12}H_{18}$ M_r = 162.27 g·mol^{-1}.

TLC R_f = 0.75 (hexanes).

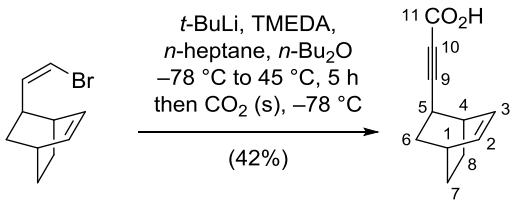
^{1}H NMR (400 MHz, $CDCl_3$): δ = 5.88 – 5.85 (ddq, $^3J_{C3\text{-}H,C4\text{-}H}$ = 6.7 Hz, $^4J_{C3\text{-}H,C1\text{-}H}$ = 2.1 Hz, $^4J_{C3\text{-}H,C11\text{-}H}$ = 1.7 Hz, 1H, C3-H), 5.77 (dd, $^3J_{C9\text{-}H,C10\text{-}Hz}$ = 17.3 Hz, $^3J_{C9\text{-}H,C10\text{-}He}$ = 10.9 Hz, 1H, C9-H), 4.80 – 4.74 (m, 2H, C10-H), 2.28 (ddddd, $^3J_{C1\text{-}H,C6\text{-}Hendo}$ = 3.8 Hz, $^3J_{C1\text{-}H,C7\text{-}Hsyn}$ = 3.8 Hz, $^3J_{C1\text{-}H,C6\text{-}Hexo}$ = 2.1 Hz, $^3J_{C1\text{-}H,C7\text{-}Hanti}$ = 2.1 Hz, $^4J_{C1\text{-}H,C3\text{-}H}$ = 2.1 Hz, 1H, C1-H), 2.06 (ddd, $^3J_{C4\text{-}H,C3\text{-}H}$ = 6.7 Hz, $^3J_{C4\text{-}H,C8\text{-}Hsyn}$ = 2.8 Hz, $^3J_{C4\text{-}H,C8\text{-}Hanti}$ = 2.8 Hz, 1H, C4-H), 1.89 (dddd, $^2J_{C8\text{-}Hanti,C8\text{-}Hsyn}$ = 12.7 Hz, $^3J_{C8\text{-}Hanti,C7\text{-}Hanti}$ = 9.6 Hz, $^3J_{C8\text{-}Hanti,C7\text{-}Hsyn}$ = 3.0, $^3J_{C8\text{-}Hanti,C4\text{-}H}$ = 3.0 Hz, 1H, C8-H_{anti}), 1.76 (d, $^4J_{C11\text{-}H,C3\text{-}H}$ = 1.7 Hz, 3H, C11-H), 1.50 – 1.41 (m, 2H, C6-H_A, C7-H_A), 1.31 – 1.20 (m, 2H, C6-H_B, C7-H_B), 1.13 (s, 3H, C12-H), 1.13 – 1.06 (m, 1H, C8-H_{syn}) ppm.

^{13}C NMR (100 MHz, $CDCl_3$): δ = 151.2 (C9), 140.7 (C2), 127.7 (C3), 108.6 (C10), 41.0 (C4), 40.6 (C6), 40.2 (C5), 36.7 (C1), 26.9 (C12), 23.8 (C7), 22.6 (C8), 20.2 (C11) ppm.

IR (ATR): $\tilde{\nu}$ = 3080 (vw), 2923 (vs), 2861 (m), 1634 (vw), 1446 (w), 1412 (vw), 1370 (vw), 1156 (vw), 1003 (vw), 906 (vs), 887 (w), 843 (vw), 821 (vw), 802 (vw), 733 (vs), 708 (vw) cm^{-1}.

HRMS (EI): m/z for $C_{12}H_{17}^+$ $[M]^+$: calcd.: 162.1403
found: 162.1383.

5-*endo*-Carboxyethinylbicyclo[2.2.2]oct-2-ene (457)



418 **457**

To a solution of alkenyl bromide **418** (107 mg, 0.500 mmol, 1.00 eq.) in *n*-heptane (4.50 mL) and *n*-Bu_2O (0.500 mL) at ─78 °C was added *t*-BuLi (2 M in *n*-pentane, 0.550 mL, 1.10 mmol, 2.20 eq.) over 5 min. The resulting mixture was stirred at ─78 °C for 15 min and then TMEDA (1.00 mL) was added. The reaction mixture was allowed to warm to room temperature and was then transferred to an oil bath at 45 °C. The reaction mixture was stirred at this temperature for 5 h and was then re-cooled to ─78 °C. Solid CO_2 was added and the reaction mixture was stirred at ─78 °C for an additional 15 min. The mixture was allowed to warm to room temperature and was then diluted with H_2O (5 mL). The

aqueous layer was washed with Et_2O (2 x 5 mL) and acidified with HCl, followed by extraction with Et_2O (5 x 10 mL). The combined organic layer from the second extraction was washed with H_2O (20 mL), brine (20 mL) and concentrated *in vacuo* to afford propiolic acid **457** (37 mg, 42%) as a colorless oil.

$C_{11}H_{12}O_2$ M_r = 176.22 g·mol^{-1}.

TLC R_f = 0.27 (hexanes : EtOAc = 3 : 1).

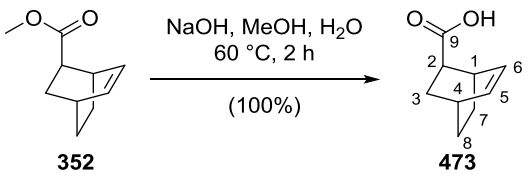
^{1}H NMR (400 MHz, $CDCl_3$): δ = 8.45 (s, 1H, CO_2H), 6.39 (ddd, $^3J_{C2\text{-}H,C3\text{-}H}$ = 8.1 Hz, $^3J_{C2\text{-}H,C1\text{-}H}$ = 6.6 Hz, $^4J_{C2\text{-}H,C4\text{-}H}$ = 1.2 Hz, 1H, C2-H), 6.26 (ddd, $^3J_{C3\text{-}H,C2\text{-}H}$ = 8.1 Hz, $^3J_{C3\text{-}H,C4\text{-}H}$ = 6.4 Hz, $^4J_{C3\text{-}H,C1\text{-}H}$ = 1.2 Hz, 1H, C3-H), 2.78 (dddd, $^3J_{C4\text{-}H,C3\text{-}H}$ = 6.4 Hz, $^3J_{C4\text{-}H,C8\text{-}Hendo}$ = 3.6 Hz, $^3J_{C4\text{-}H,C5\text{-}H}$ = 2.3 Hz, $^4J_{C4\text{-}H,C2\text{-}H}$ = 1.2 Hz, 1H, C4-H), 2.72 (ddd, $^3J_{C5\text{-}H,C6\text{-}Hexo}$ = 10.0 Hz, $^3J_{C5\text{-}H,C6\text{-}Hendo}$ = 4.9 Hz, $^3J_{C5\text{-}H,C4\text{-}H}$ = 2.3 Hz, 1H, C5-H), 2.59 (dddddd, $^3J_{C1\text{-}H,C2\text{-}H}$ = 6.6 Hz, $^3J_{C1\text{-}H,C7\text{-}Hendo}$ = 3.4 Hz, $^3J_{C1\text{-}H,C6\text{-}Hendo}$ = 3.4 Hz, $^3J_{C1\text{-}H,C7\text{-}Hexo}$ = 2.5 Hz, $^3J_{C1\text{-}H,C6\text{-}Hexo}$ = 2.5 Hz, $^4J_{C1\text{-}H,C3\text{-}H}$ = 1.2 Hz, 1H, C1-H), 1.95 (ddd, $^2J_{C6\text{-}Hexo,C6\text{-}Hendo}$ = 12.5 Hz, $^3J_{C6\text{-}Hexo,C5\text{-}H}$ = 10.0 Hz, $^3J_{C6\text{-}Hexo,C1\text{-}H}$ = 2.5 Hz, 1H, C6-H_{exo}), 1.52 (dddd, $^2J_{C8\text{-}Hexo,C8\text{-}Hendo}$ = 13.7 Hz, $^3J_{C8\text{-}Hexo,C7\text{-}Hexo}$ = 9.1 Hz, $^3J_{C8\text{-}Hexo,C7\text{-}Hendo}$ = 2.5 Hz, 1H, C8-H_{exo}), 1.47 – 1.39 (m, 2H, C6-H_{endo}, C7-H_{exo}), 1.32 – 1.21 (m, 2H, C7-H_{endo}, C8-H_{endo}) ppm.

^{13}C NMR (100 MHz, $CDCl_3$): δ = 158.6 (C11), 135.8 (C2), 131.7 (C3), 97.5 (C9), 71.0 (C10), 34.3 (C4), 34.1 (C6), 29.2 (C1*), 29.1 (C5*), 25.2 (C8), 23.9 (C7) ppm.

IR (ATR): $\tilde{\nu}$ = 3430 (vw), 3300 (vw), 3042 (w), 2938 (vs), 2865 (s), 1709 (vs), 1463 (w), 1451 (w), 1374 (w), 1364 (w), 1309 (m), 1244 (s), 1172 (s), 1093 (m), 1069 (m), 1046 (m), 989 (w), 914 (w), 854 (w), 815 (w), 708 (s) cm^{-1}.

HRMS (ESI–): m/z for $C_{11}H_{11}O_2^-$ $[M–H]^-$: calcd.: 175.0765
found: 175.0763.

Bicyclo[2.2.2]oct-5-ene-2-*endo*-carboxylic acid (473)



352 **473**

To a solution of bicycloester **352** (13.7 g, 82.3 mmol, 1.00 eq.) in methanol (250 mL) was added aqueous NaOH (10 wt-%, 65.0 mL). The reaction mixture was heated to 60 °C for 2 h, was then allowed to cool to room temperature and was acidified with 1 M HCl. The reaction mixture was extracted with CH_2Cl_2 (3 x 300 mL, 200 mL). The combined organic layer was dried (Na_2SO_4) and concentrated *in vacuo* to afford carboxylic acid **473** (12.5 g, 100 %) as a colorless solid.

$C_9H_{12}O_2$ M_r = 152.19 g·mol^{-1}.

TLC R_f = 0.35 (hexanes : EtOAc = 3 : 1).

mp 55 – 57 °C.

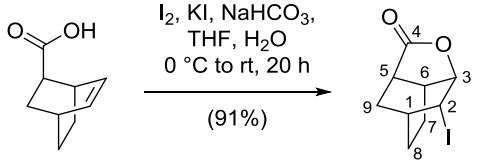
^{1}H NMR (300 MHz, $CDCl_3$): δ = 12.43 – 10.55 (br s, 1H, OH), 6.35 (ddd, $^3J_{C5\text{-}H,C6\text{-}H}$ = 8.0 Hz, $^3J_{C5\text{-}H,C4\text{-}H}$ = 6.7 Hz, $^4J_{C5\text{-}H,C1\text{-}H}$ = 1.2 Hz, 1H, C5-H), 6.20 (ddd, $^3J_{C6\text{-}H,C5\text{-}H}$ = 8.0 Hz, $^3J_{C6\text{-}H,C1\text{-}H}$ = 6.4 Hz, $^4J_{C6\text{-}H,C4\text{-}H}$ = 1.2 Hz, 1H, C6-H), 3.03 – 2.95 (m, 1H, C1-H), 2.69 (ddd, $^3J_{C2\text{-}H,C3\text{-}Hexo}$ = 9.7 Hz, $^3J_{C2\text{-}H,C3\text{-}Hendo}$ = 5.5 Hz, $^3J_{C2\text{-}H,C1\text{-}H}$ = 2.3 Hz, 1H, C2-H), 2.65 – 2.59 (m, 1H, C4-H), 1.82 – 1.66 (m, 2H, C3-H), 1.62 – 1.46 (m, 2H, C7-H_{syn}, C8-H_{syn}), 1.36 – 1.24 (m, 2H, C7-H_{anti}, C8-H_{anti}) ppm.

^{13}C NMR (75 MHz, $CDCl_3$): δ = 181.8 (C9), 135.5 (C5), 131.5 (C6), 42.8 (C2), 32.5 (C1), 29.7 (C3), 29.5 (C4), 25.5 (C7), 24.5 (C8) ppm.

IR (ATR): $\tilde{\nu}$ = 3045 (w), 2939 (m), 2867 (m), 2726 (w), 2627 (w), 1695 (vs), 1450 (w), 1409 (w), 1373 (w), 1346 (w), 1317 (m), 1287 (w), 1232 (vs), 1176 (m), 1120 (w), 1082 (w), 1051 (w), 1019 (w), 906 (s), 862 (m), 833 (w), 817 (w), 797 (w), 749 (w), 696 (vs) cm^{-1}.

HRMS (EI): m/z for $C_9H_{12}O_2^+$ $[M]^+$: calcd.: 152.0832
found: 152.0840.

2-Iodo-4-oxatricyclo[4.3.1.0^{3,7}]decan-5-one (474)



473 **474**

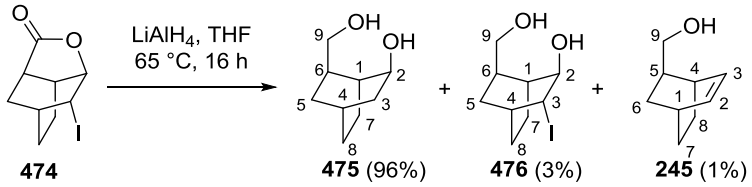
To a solution of unsaturated carboxylic acid **473** (0.761 g, 5.00 mmol, 1.00 eq.) in a mixture of saturated aqueous $NaHCO_3$ (9.00 mL) and THF (33.0 mL) at 0 °C was added a mixture of KI (4.98 g), I_2 (2.54 g) in H_2O (21.5 mL) over a period of 1 h. The reaction mixture was allowed to warm to room temperature and stirred at this temperature for an additional 20 h. The reaction was quenched by addition of saturated aqueous $Na_2S_2O_3$. The layers were separated and the aqueous layer was extracted with EtOAc (3 x 40 ml). The combined organic layers were washed with 1 M NaOH (20 mL), brine (20 mL), dried (Na_2SO_4) and concentrated *in vacuo*. Purification of the residue by flash column chromatography (4 x 24 cm, silica, hexanes : EtOAc = gradient from 9 : 1 to 4 : 1, 20 mL, #54–80) afforded iodolactone **474** as a colorless solid (1.26 g, 91%). Recrystallization from CH_2Cl_2 afforded crystals suitable for single crystal X-ray diffraction.

$C_9H_{11}IO_2$ M_r = 278.09 g·mol^{-1}.

TLC R_f = 0.43 (hexanes : EtOAc = 9 : 1).

mp	91 – 93 °C.
^{1}H NMR	(300 MHz, $CDCl_3$): δ = 5.02 – 4.96 (m, 1H, C3-H), 4.40 – 4.35 (m, 1H, C2-H), 2.59 – 2.47 (m, 2H, C5-H, C6-H), 2.20 – 2.08 (m, 3H, C1-H, C8-H_{exo}*, C9-H_{syn}**), 2.00 – 1.86 (m, 3H, C7-H, C9-H_{anti}**), 1.66 – 1.55 (m, 1H, C8-H_{endo}*) ppm.
^{13}C NMR	(75 MHz, $CDCl_3$): δ = 179.5 (C4), 85.8 (C3), 35.7 (C5), 34.6 (C6), 32.1 (C1), 29.8 (C2), 28.2 (C9), 24.2 (C8), 15.0 (C7) ppm.
IR	(ATR): $\tilde{\nu}$ = 2939 (w), 1765 (s), 1468 (w), 1450 (w), 1372 (w), 1346 (w), 1332 (m), 1313 (w), 1291 (w), 1271 (w), 1209 (w), 1184 (m), 1156 (w), 1142 (m), 1099 (w), 1077 (m), 1047 (s), 1018 (w), 970 (s), 958 (vs), 942 (s), 892 (m), 846 (m), 814 (w), 760 (m), 731 (m), 656 (m) cm^{-1}.
HRMS	(EI): m/z for $C_9H_{11}IO_2^+$ $[M]^+$: calcd.: 277.9798 found: 277.9800.

Reduction of Iodolactone 474



To a refluxing solution of $LiAlH_4$ (9.77 g, 258 mmol, 5.00 eq.) in THF (400 mL) was added dropwise a solution of iodolactone **474** (14.3 g, 51.5 mmol, 1.00 eq.) in THF (150 mL). After complete addition the reaction mixture was refluxed for an additional 16 h and was then cooled to 0 °C. Excess $LiAlH_4$ was hydrolyzed by addition of saturated aqueous Na_2SO_4 (150 mL) which after initial gas evolution, lead to the formation of a white precipitate. 1 M HCl (300 mL) was added to provide a homogeneous solution. The reaction mixture was extracted with EtOAc (3 x 500 mL). The combined organic layer was washed with brine (450 mL), dried (Na_2SO_4) and concentrated *in vacuo*. Purification of the residue by flash column chromatography (10 x 20 cm, silica, hexanes : EtOAc = 1 : 1, 20 mL) afforded hydroxybicyclooctene **245** (0.120 g, 1%, #7–9) as a colorless oil, iodohydrine **476** (0.500 g, 3%, #17–23) as a colorless solid and desired diol **475** (7.83 g, 96%, #30–55) as a colorless solid. Recrystallization of iodohydrine **476** from CH_2Cl_2/hexanes afforded crystals suitable for single crystal X-ray diffraction.

*2-endo-Hydroxy-6-endo-hydroxymethylbicyclo[2.2.2]octane (**475**)*

$C_9H_{16}O_2$ M_r = 156.22 g·mol^{-1}.

TLC R_f = 0.08 (hexanes : EtOAc = 3 : 1).

mp 55 – 57 °C.

^{1}H NMR (300 MHz, $CDCl_3$): δ = 5.00 (br s, 2H, C2-OH, C5-OH), 3.90 – 3.77 (m, 1H, C2-H), 3.55 (d, $^2J_{C9\text{-}H,C6\text{-}H}$ = 4.2 Hz, 2H, C9-H), 1.98 – 1.86 (m, 1H, C3-H_{exo}), 1.86 – 1.74 (m, 1H, C6-H), 1.71 – 1.64 (m, 1H, C4-H), 1.64 – 1.59 (m, 1H, C1-H), 1.56 – 1.42 (m, 4H, C5-H, C7-H), 1.42 – 1.25 (m, 3H, C3-H_{endo}, C8-H) ppm.

^{13}C NMR (75 MHz, $CDCl_3$): δ = 69.1 (C2), 65.4 (C9), 38.0 (C3), 37.4 (C6), 36.0 (C1), 28.4 (C5), 26.3 (C7), 25.0 (C4), 23.7 (C8) ppm.

IR (ATR): $\tilde{\nu}$ = 3247 (w), 2932 (m), 2864 (m), 2242 (vw), 1715 (vw), 1663 (vw), 1453 (w), 1363 (vw), 1298 (vw), 1280 (vw), 1233 (vw), 1215 (vw), 1145 (vw), 1100 (m), 1027 (s), 985 (m), 907 (m), 832 (w), 809 (w), 783 (w), 728 (vs) cm^{-1}.

HRMS (ESI+): m/z for $C_9H_{17}O_2^+$ $[M+H]^+$: calcd.: 157.1223
found: 157.1224.

*2-endo-Hydroxy-6-endo-hydroxymethyl-3-exo-iodobicyclo[2.2.2]octane (**476**)*

$C_9H_{15}IO_2$ M_r = 282.12 g·mol^{-1}.

TLC R_f = 0.28 (hexanes : EtOAc = 3 : 1).

mp 99 – 101 °C.

^{1}H NMR (600 MHz, $CDCl_3$): δ = 4.27 – 4.21 (m, 2H, C2-H, C3-H), 3.79 (br s, 2H, C2-OH, C9-OH), 3.65 (dd, $^2J_{C9\text{-}HA,C9\text{-}HB}$ = 11.1 Hz, $^3J_{C9\text{-}HA,C6\text{-}H}$ = 3.2 Hz, 1H, C9-H_A*), 3.59 (dd, $^2J_{C9\text{-}HB,C9\text{-}HA}$ = 11.1 Hz, $^3J_{C9\text{-}HB,C6\text{-}H}$ = 5.4 Hz, 1H, C9-H_B*), 2.03 – 2.00 (m, 1H, C4-H), 1.97 – 1.85 (m, 2H, C6-H, C8-H_{syn}**), 1.79 – 1.70 (m, 3H, C5-H, C7-H_{syn}***), 1.66 – 1.62 (m, 1H, C1-H), 1.61 – 1.49 (m, 2H, C7-H_{anti}***, C8-H_{anti}**) ppm.

^{13}C NMR (150 MHz, $CDCl_3$): δ = 82.2 (C2), 65.4 (C9), 42.0 (C3), 37.3 (C1), 36.5 (C4), 36.1 (C6), 29.3 (C5), 26.4 (C7), 21.3 (C8) ppm.

IR (ATR): $\tilde{\nu}$ = 3225 (w), 2933 (m), 2866 (m), 2360 (vw), 2240 (vw), 1466 (w), 1447 (w), 1355 (w), 1312 (w), 1248 (w), 1211 (w), 1191 (w), 1144 (w), 1107 (m), 1084 (m), 1073 (m), 1058 (m), 1036 (vs), 983 (s), 944 (w), 919 (s), 729 (vs), 662 (s) cm^{-1}.

HRMS (ESI+): m/z for $C_9H_{16}IO_2$ $[M+H]^+$: calcd.: 283.0190
found: 283.0190.

*5-endo-Hydroxymethylbicyclo[2.2.2]oct-2-ene (**245**)*

$C_9H_{14}O$ M_r = 138.21 g·mol^{-1}.

TLC R_f = 0.44 (hexanes : EtOAc = 1 : 1).

^{1}H NMR (300 MHz, $CDCl_3$): δ = 6.27 (ddd, $^3J_{C2\text{-}H,C3\text{-}H}$ = 8.0 Hz, $^3J_{C2\text{-}H,C1\text{-}H}$ = 6.6 Hz, $^4J_{C2\text{-}H,C4\text{-}H}$ = 1.2 Hz, 1H, C2-H), 6.16 – 6.09 (m, 1H, C3-H), 3.28 – 3.21 (m, 2H, C9-H), 2.63 – 2.57 (m, 1H, C4-H), 2.53 – 2.45 (m, 1H, C1-H), 1.93 – 1.86 (m, 1H,

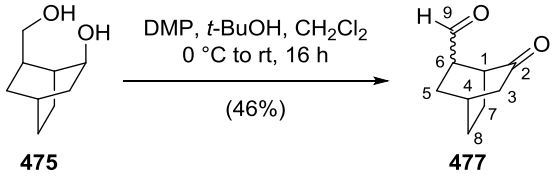
C5-H), 1.67 (ddd, $^2J_{C6\text{-}Hexo,C6\text{-}Hendo}$ = 12.2 Hz, $^3J_{C6\text{-}Hexo,C5\text{-}H}$ = 9.5 Hz, $^3J_{C6\text{-}Hexo,C1\text{-}H}$ = 2.7 Hz, 1H, C6-H_{exo}), 1.55 – 1.45 (m, 2H, C7-H_{anti}, C8-H_{anti}), 1.32 – 1.21 (m, 2H, C7-H_{syn}, C8-H_{syn}), 0.80 – 0.70 (m, 1H, C6-H_{endo}) ppm.

^{13}C NMR (75 MHz, $CDCl_3$): δ = 135.2 (C2), 131.9 (C3), 67.7 (C9), 40.7 (C5), 31.5 (C4), 30.3 (C6), 29.9 (C1), 26.1 (C8), 24.9 (C7) ppm.

IR (ATR): $\tilde{\nu}$ = 3315 (w), 3040 (vw), 2933 (s), 2862 (m), 2361 (vw), 2333 (vw), 1637 (vw), 1613 (vw), 1463 (w), 1450 (w), 1376 (w), 1269 (vw), 1207 (vw), 1181 (vw), 1109 (vw), 1049 (m), 1029 (s), 1012 (m), 973 (w), 900 (w), 851 (w), 809 (w), 788 (vw), 733 (w), 702 (vs) cm^{-1}.

HRMS (EI): m/z for $C_9H_{14}O^+$ $[M]^+$: calcd.: 138.1039
found: 138.1048.

6-Formylbicyclo[2.2.2]octan-2-one (477)



475 **477**

To a solution of diol **475** (1.00 g, 6.40 mmol, 1.00 eq.) and *tert*-butanol (0.024 g, 0.320 mmol, 0.050 eq.) in CH_2Cl_2 (100 mL) at 0 °C was added DMP (8.14 g, 19.2 mmol, 3.00 eq.) in one portion and the resulting mixture was stirred at room temperature for 16 h. The reaction was quenched by addition of a 1 : 1 mixture of saturated aqueous $NaHCO_3$ and saturated aqueous $Na_2S_2O_3$ (250 mL). The resulting mixture was stirred until a clear two-phasic solution was obtained. The layers were separated and the aqueous layer was extracted with CH_2Cl_2 (2 x 150 mL). The combined organic layer was dried (Na_2SO_4) and concentrated *in vacuo*. The residue was purified by flash column chromatography (4 x 20 cm, silica, *n*-pentane : Et_2O = 1 : 1 to 2 : 3, 20 mL, #33–85) to afford an unseparable *endo*,*exo*-mixture of keto aldehyde **477** (450 mg, 46%) in form of a colorless oil.

$C_9H_{12}O_2$ M_r = 152.19 g·mol^{-1}.

TLC R_f = 0.58 (hexanes : EtOAc = 1 : 1).

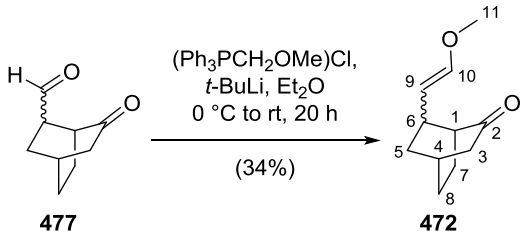
^{1}H NMR (300 MHz, $CDCl_3$, both isomers): δ = 9.74 – 9.59 (m, 1H, C9-H), 2.94 – 2.77 (m, 1H, C6-H), 2.77 – 2.64 (m, 1H, C1-H), 2.35 – 1.52 (m, 9H, C3-H, C4-H, C5-H, C7-H, C8-H) ppm.

^{13}C NMR (75 MHz, $CDCl_3$, both isomers): δ = 214.3 (C2), 213.8 (C2), 201.3 (C9), 201.2 (C9), 48.7 (C6), 46.1 (C6), 44.8 (C3), 44.5 (C3), 43.0 (C1), 42.2 (C1), 27.9 (C4), 27.4 (C4), 24.8 (C5*), 24.4 (C7*), 24.3 (C5*), 24.3 (C8*), 23.4 (C7*), 19.2 (C8*) ppm.

IR (ATR): $\tilde{\nu}$ = 2932 (w), 2870 (w), 1715 (vs), 1453 (w), 1400 (w), 1329 (w), 1222 (w), 1144 (m), 1070 (s), 989 (m), 885 (w), 860 (w), 818 (w) cm^{-1}.

HRMS (EI): m/z for $C_9H_{12}O_2^+$ $[M]^+$: calcd.: 152.0832
found: 152.0829.

6-(2-Methoxyalkenyl)bicyclo[2.2.2]octan-2-one (472)



477 **472**

To a suspension of (methoxymethyl)triphenylphosphonium chloride (0.475 g, 1.39 mmol, 1.05 eq.) in Et_2O (8.25 mL) at 0 °C was added *t*-BuLi (1.7 M in *n*-pentane, 0.776 mL, 1.32 mmol, 1.00 eq.). The resulting mixture was stirred for 90 min at 0 °C and then a solution of keto aldehyde **477** (0.201 g, 1.32 mmol, 1.00 eq.) in Et_2O (1.65 mL) was added dropwise at 0 °C. The resulting mixture was slowly warmed to room temperature and stirred at this temperature for 20 h. The reaction mixture was poured into saturated aqueous NH_4Cl (30 mL) and extracted with Et_2O (3 x 10 mL). The organic layer was washed with brine (20 mL), dried ($MgSO_4$) and concentrated *in vacuo*. Purification of the residue by flash column chromatography (3 x 15 cm, silica, hexanes : Et_2O = 3 : 1, 20 mL, #13–18) afforded an unseparable *endo*,*exo*-mixture of (*E*)-enolether **472** (81 mg, 34%) in form of a colorless oil.

$C_{11}H_{16}O_2$ M_r = 180.25 g·mol^{-1}.

TLC R_f = 0.43 (hexanes : EtOAc = 3 : 1).

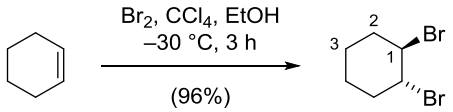
^{1}H NMR (300 MHz, $CDCl_3$, both isomers): δ = 6.37 – 6.26 (m, 1H, C10-H), 4.87 – 4.44 (m, 1H, C9-H), 3.54 – 3.44 (m, 3H, C11-H), 2.59 – 2.46 (m, 1H, C6-H), 2.18 (m, 4H, C1-H, C3-H, C4-H), 2.09 – 1.24 (m, 6H, C5-H, C7-H, C8-H) ppm.

^{13}C NMR (75 MHz, $CDCl_3$, major isomer): δ = 216.6 (C2), 147.1 (C10), 107.3 (C9), 56.0 (C11), 49.7 (C1), 45.1 (C3), 35.9 (C6), 34.8 (C5), 28.1 (C4), 23.7 (C7*), 23.4 (C8*) ppm.

IR (ATR): $\tilde{\nu}$ = 2936 (m), 2869 (w), 2833 (vw), 2360 (vw), 2333 (vw), 1719 (vs), 1670 (w), 1652 (s), 1465 (vw), 1454 (w), 1403 (vw), 1340 (vw), 1314 (vw), 1208 (m), 1148 (m), 1128 (w), 1112 (w), 1098 (w), 1072 (vw), 1054 (vw), 993 (vw), 933 (w), 888 (vw), 867 (vw), 800 (vw), 740 (vw), 696 (vw) cm^{-1}.

HRMS (EI): m/z for $C_{11}H_{16}O_2^+$ $[M]^+$: calcd.: 180.1145
found: 180.1152.

1,2-Dibromocyclohexane (480)



479 **480**

To a solution of cyclohexene (**479**) (304 mL, 246 g, 3.00 mol, 1.00 eq.) in CCl_4 (600 mL) and EtOH (30.0 mL) at −30 °C was added bromine (138 mL, 431 g, 2.70 mol, 0.900 eq.) at such a rate that the temperature did not rise above −15 °C. After complete addition the flask was equipped with a distillation head and CCl_4 and excess cyclohexene (**479**) were removed from the reaction mixture. The crude product was submitted to distillation at 16 mbar and 100 °C to afford dibromocyclohexane **480** (626 g, 96%) as a colorless oil.

$C_6H_{10}Br_2$ M_r = 241.95 g·mol^{-1}.

TLC R_f = 0.63 (hexanes).

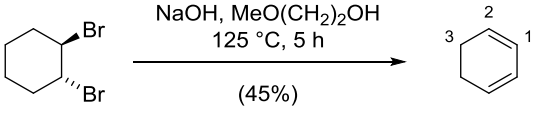
^{1}H NMR (300 MHz, $CDCl_3$): δ = 4.68 – 4.88 (m, 2H, C1-H), 2.55 – 2.31 (m, 2H, C2-H_A), 2.03 – 1.71 (m, 4H, C2-H_B, C3-H_A), 1.61 – 1.44 (m, 2H, C3-H_B) ppm.

^{13}C NMR (75 MHz, $CDCl_3$): δ = 55.3 (C1), 32.1 (C2), 22.6 (C3) ppm.

IR (ATR): $\tilde{\nu}$ = 2937 (m), 2860 (m), 1445 (m), 1431 (s), 1258 (w), 1336 (w), 1319 (w), 1267 (w), 1256 (w), 1195 (w), 1177 (vs), 1160 (m), 1136 (w), 1116 (w), 1059 (w), 1048 (w), 1032 (w), 998 (s), 972 (m), 902 (m), 860 (m), 840 (w), 811 (m), 696 (m), 685 (s), 663 (vs) cm^{-1}.

HRMS (EI): m/z for $C_6H_{10}Br_2^+$ $[M]^+$: calcd.: 239.9144
found: 239.9130.

1,3-Cyclohexadiene (243)

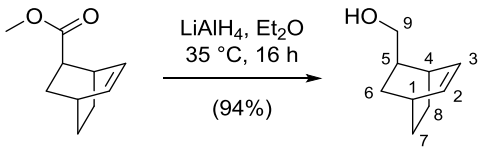


480 **243**

In a round bottom flask equipped with a pressure equalizing dropping funnel and a distillation head, NaOH (316 g, 7.90 mol, 3.05 eq.) was dissolved in 2-methoxyethanol (720 mL). The mixture was heated to 125 °C and at this temperature dibromocyclohexane **480** (351 mL, 627 g, 2.59 mol, 1.00 eq.) was added dropwise. Cyclohexadiene **243** was distilled directly out of the reaction mixture as an azeotropic mixture with H_2O. The layers of the distillate were separated and the organic layer was dried (Na_2SO_4) and distilled to afford cyclohexadiene **243** (92.5 g, 45%) contaminated with some benzene as a colorless oil.

C_6H_8	M_r = 80.13 g·mol^{-1}.
TLC	R_f = 0.99 (hexanes).
^{1}H NMR	(300 MHz, $CDCl_3$): δ = 5.94 – 5.86 (m, 2H, C3-H), 5.84 – 5.76 (m, 2H, C2-H), 2.18 – 2.13 (m, 4H, C1-H) ppm.
^{13}C NMR	(75 MHz, $CDCl_3$): δ = 126.4 (C2), 124.4 (C3), 22.2 (C1) ppm.
IR	(ATR): $\tilde{\nu}$ = 3045 (w), 2940 (m), 2866 (m), 1809 (w), 1729 (vs), 1452 (w), 1373 (m), 1316 (m), 1288 (w), 1189 (s), 1172 (vs), 1110 (w), 1081 (m), 1051 (m), 989 (m), 909 (m), 866 (w), 839 (w), 746 (w), 698 (s) cm^{-1}.
HRMS	(EI): m/z for $C_6H_8^+$ $[M]^+$: calcd.: 80.0621 found: 80.0608.

5-*endo*-Hydroxymethylbicyclo[2.2.2]oct-2-ene (245)

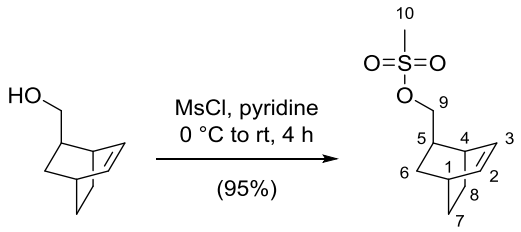


352 **245**

To a solution of $LiAlH_4$ (2.50 g, 66.0 mmol, 0.600 eq.) in Et_2O (130 mL) was added dropwise a solution of bicycloester **352** (18.3 g, 110 mmol, 1.00 eq.) in Et_2O (25.0 mL). After complete addition the reaction mixture was heated to 35 °C for 16 h and was then cooled to 0 °C. Excess $LiAlH_4$ was hydrolyzed by dropwise addition of H_2O. Rochelle salt was added until a homogeneous solution was obtained. The aqueous layer was extracted with Et_2O (4 x 50 mL) and the combined organic layer was washed with H_2O (75 mL), brine (75 mL), dried (Na_2SO_4) and concentrated *in vacuo*. Purification of the residue by flash column chromatography (10 x 20 cm, silica, hexanes : Et_2O = 2 : 1, 100 mL, #28–68) afforded bicyclooctenol **245** (14.3 g, 94%) as a colorless oil.

See above for analytical data.

5-*endo*-Mesyloxymethylbicyclo[2.2.2]oct-2-ene (246)



245 **246**

To a solution of bicyclic alcohol **245** (14.4 g, 104 mmol, 1.00 eq.) in pyridine (26.0 mL) at 0 °C was added dropwise MsCl (8.85 mL, 13.1 g, 114 mmol, 1.10 eq.). The resulting reaction mixture was allowed to warm to room temperature and allowed to stand at this temperature for 4 h after which time H_2O (6 mL) was added. The reaction mixture was poured into H_2O (50 mL) and extracted with Et_2O (3 x 75 mL). The combined organic layer was washed with 1 M HCl (100 mL), H_2O (100 mL), brine (100 mL), dried (Na_2SO_4) and concentrated *in vacuo*. Purification of the residue by flash column chromatography (10 x 13 cm, silica, hexanes : EtOAc = 9 : 1, 100 mL, #24–45) afforded mesylate **246** (21.4 g, 95%) as a colorless oil.

$C_{10}H_{16}O_3S$ M_r = 216.30 g·mol^{-1}.

TLC R_f = 0.19 (hexanes : EtOAc = 9 : 1).

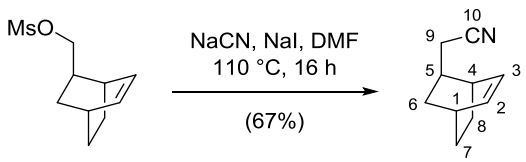
^{1}H NMR (600 MHz, $CDCl_3$): δ = 6.33 – 6.29 (m, 1H, C2-H), 6.14 – 6.10 (m, 1H, C3-H), 3.81 – 3.79 (m, 2H, C9-H), 2.98 (s, 3H, C10-H), 2.65 – 2.61 (m, 1H, C4-H), 2.55 – 2.51 (m, 1H, C1-H), 2.18 – 2.11 (m, 1H, C5-H), 1.72 (ddd, $^2J_{C6\text{-}Hexo,C6\text{-}Hendo}$ = 12.6 Hz, $^3J_{C6\text{-}Hexo,C5\text{-}H}$ = 9.7 Hz, $^3J_{C6\text{-}Hexo,C1\text{-}H}$ = 2.7 Hz, 1H, C6-H_{exo}), 1.55 – 1.47 (m, 2H, C7-H_{anti}, C8-H_{anti}), 1.33 – 1.25 (m, 2H, C7-H_{syn}, C8-H_{syn}), 0.74 (dddd, $^2J_{C6\text{-}Hendo,C6\text{-}Hexo}$ = 12.8 Hz, $^3J_{C6\text{-}Hendo,C5\text{-}H}$ = 5.3 Hz, $^3J_{C6\text{-}Hendo,C1\text{-}H}$ = 3.1 Hz, $^4J_{C6\text{-}Hendo,C7\text{-}Hsyn}$ = 3.1 Hz, 1H, C6-H_{endo}) ppm.

^{13}C NMR (150 MHz, $CDCl_3$): δ = 135.6 (C2), 131.2 (C3), 73.6 (C9), 37.4 (C5), 37.4 (C10), 31.0 (C4), 29.6 (C1), 29.6 (C6), 25.4 (C8), 24.6 (C7) ppm.

IR (ATR): $\tilde{\nu}$ = 3042 (vw), 2940 (w), 2866 (w), 1464 (vw), 1415 (vw), 1351 (vs), 1229 (vw), 1172 (vs), 1043 (vw), 981 (m), 946 (vs), 904 (w), 868 (w), 840 (m), 814 (m), 746 (vw), 706 (w) cm^{-1}.

HRMS (EI): m/z for $C_{10}H_{16}O_3S^+$ $[M]^+$: calcd.: 216.0815
found: 216.0814.

5-*endo*-Cyanomethylbicyclo[2.2.2]oct-2-ene (247)



246 **247**

Mesylate **246** (22.5 g, 104 mmol, 1.00 eq.) was dissolved in DMF (46.0 mL) and NaCN (11.3 g, 231 mmol, 2.22 eq.) and NaI (0.363 g, 2.42 mmol, 0.023 eq.) were added and the mixture was heated to 110 °C for 16 h. The reaction mixture was allowed to cool to room temperature and was then poured into H_2O (100 mL). The aqueous layer was extracted with hexanes (3 x 100 mL). The combined organic layer was washed with H_2O (150 mL), brine (150 mL), dried (Na_2SO_4) and concentrated *in vacuo*. Purification of the residue by flash column chromatography (10 x 25 cm, silica, hexanes : Et_2O = 9 : 1 to 4 : 1, 100 mL, #22–47) afforded nitrile **247** (10.3 g, 67%) as a colorless oil.

$C_{10}H_{13}N$ M_r = 147.22 g·mol^{-1}.

TLC R_f = 0.41 (hexanes : EtOAc = 9 : 1).

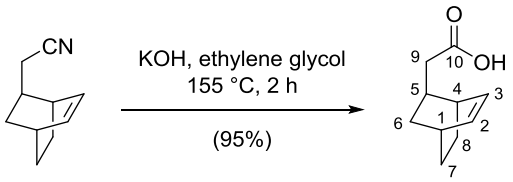
^{1}H NMR (600 MHz, $CDCl_3$): δ = 6.33 (ddd, $^3J_{C2\text{-}H,C3\text{-}H}$ = 8.0 Hz, $^3J_{C2\text{-}H,C1\text{-}H}$ = 6.7 Hz, $^3J_{C2\text{-}H,C4\text{-}H}$ = 1.0 Hz, 1H, C2-H), 6.14 – 6.10 (m, 1H, C3-H), 2.59 – 2.56 (m, 1H, C4-H), 2.56 – 2.52 (m, 1H, C1-H), 2.12 – 2.04 (m, 3H, C5-H, C9-H), 1.88 – 1.83 (m, 1H, C6-H_{exo}), 1.54 (dddd, $^2J_{C8\text{-}Hanti,C8\text{-}Hsyn}$ = 12.1 Hz, $^3J_{C8\text{-}Hanti,C7\text{-}Hanti}$ = 9.8 Hz, $^3J_{C8\text{-}Hanti,C7\text{-}Hsyn}$ = 4.0 Hz, $^3J_{C8\text{-}Hanti,C4\text{-}H}$ = 2.5 Hz, 1H, C8-H_{anti}), 1.45 (dddd, $^2J_{C7\text{-}Hanti,C7\text{-}Hsyn}$ = 12.0 Hz, $^3J_{C7\text{-}Hanti,C8\text{-}Hanti}$ = 9.8 Hz, $^3J_{C7\text{-}Hanti,C8\text{-}Hsyn}$ = 4.2 Hz, $^3J_{C7\text{-}Hanti,C1\text{-}H}$ = 2.3 Hz, 1H, C7-H_{anti}), 1.34 (dddd, $^2J_{C8\text{-}Hsyn,C8\text{-}Hanti}$ = 12.1 Hz, $^3J_{C8\text{-}Hsyn,C7\text{-}Hsyn}$ = 12.0 Hz, $^3J_{C8\text{-}Hsyn,C7\text{-}Hanti}$ = 4.2 Hz, $^3J_{C8\text{-}Hsyn,C4\text{-}H}$ = 3.4 Hz, 1H, C8-H_{syn}), 1.22 (ddddd, $^2J_{C7\text{-}Hsyn,C7\text{-}Hanti}$ = 12.0 Hz, $^3J_{C7\text{-}Hsyn,C8\text{-}Hsyn}$ = 12.0 Hz, $^3J_{C7\text{-}Hsyn,C8\text{-}Hanti}$ = 4.0 Hz, $^3J_{C7\text{-}Hsyn,C1\text{-}H}$ = 3.1 Hz, $^4J_{C7\text{-}Hsyn,C6\text{-}Hendo}$ = 3.1 Hz, 1H, C7-H_{syn}), 0.86 – 0.81 (m, 1H, C6-H_{endo}) ppm.

^{13}C NMR (150 MHz, $CDCl_3$): δ = 135.9 (C2), 130.7 (C3), 119.6 (C10), 34.9 (C5), 34.0 (C4), 33.3 (C6), 29.9 (C1), 25.7 (C8), 24.5 (C9), 24.1 (C7) ppm.

IR (ATR): $\tilde{\nu}$ = 3044 (vw), 2937 (vs), 2866 (m), 2245 (vw), 1452 (vw), 1425 (w), 1376 (w), 1353 (vw), 1314 (vw), 1165 (vw), 1095 (vw), 941 (vw), 887 (vw), 845 (vw), 809 (vw), 707 (vs) cm^{-1}.

HRMS (EI): m/z for $C_{10}H_{13}N^+$ $[M]^+$: calcd.: 147.1043
found: 147.1034.

5-*endo*-Carboxymethylbicyclo[2.2.2]oct-2-ene (248)



247 **248**

A mixture of nitrile **247** (10.3 g, 69.7 mmol, 1.00 eq.) and KOH (7.82 g, 139 mmol, 2.00 eq.) in ethylene glycol (40.0 mL) was heated to 155 °C and stirred at this temperature for 2 h. The reaction mixture was allowed to cool to room temperature, was diluted with H_2O (100 mL) and extracted with Et_2O (100 mL). The aqueous layer was acidified (1 M HCl) and extracted with Et_2O (8 x 100 mL). The combined organic layer was washed with H_2O (200 mL), brine (200 mL), dried (Na_2SO_4) and concentrated *in vacuo* to afford bicyclic acid **248** (11.0 g, 95%) as a colorless solid.

$C_{10}H_{14}O_2$ M_r = 166.22 g·mol^{-1}.

TLC R_f = 0.16 (hexanes : EtOAc = 9 : 1).

mp 39 – 41 °C.

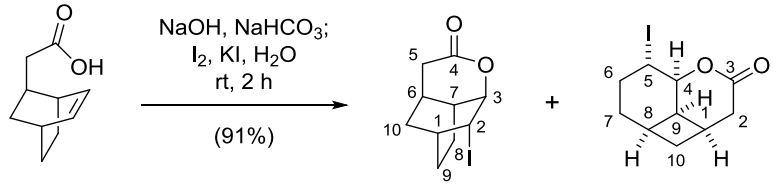
^{1}H NMR (600 MHz, $CDCl_3$): δ = 6.31 – 6.27 (m, 1H, C2-H), 6.14 – 6.10 (m, 1H, C3-H), 2.50 – 2.46 (m, 1H, C1-H), 2.45 – 2.42 (m, 1H, C4-H), 2.21 (dd, $^3J_{C9\text{-}Ha,C9\text{-}Hb}$ = 14.4 Hz, $^3J_{C9\text{-}Ha,C5\text{-}H}$ = 7.0 Hz, 1H, C9-H_A), 2.18 – 2.12 (m, 1H, C5-H), 2.07 (dd, $^2J_{C9\text{-}Hb,C9\text{-}Ha}$ = 14.4 Hz, $^3J_{C9\text{-}Hb,C5\text{-}H}$ = 7.3 Hz, 1H, C9-H_B), 1.83 (ddd, $^2J_{C6\text{-}Hexo,C6\text{-}Hendo}$ = 12.5 Hz, $^3J_{C6\text{-}Hexo,C5\text{-}H}$ = 9.2 Hz, $^3J_{C6\text{-}Hexo,C1\text{-}H}$ = 2.7 Hz, 1H, C6-H_{exo}), 1.55 (dddd, $^3J_{C8\text{-}Hanti,C8\text{-}Hsyn}$ = 12.3 Hz, $^3J_{C8\text{-}Hanti,C7\text{-}Hanti}$ = 9.8 Hz, $^3J_{C8\text{-}Hanti,C7\text{-}Hsyn}$ = 3.9 Hz, $^3J_{C8\text{-}Hanti,C4\text{-}H}$ = 2.6 Hz, 1H, C8-H_{anti}), 1.45 (dddd, $^2J_{C7\text{-}Hanti,C7\text{-}Hsyn}$ = 11.8 Hz, $^3J_{C7\text{-}Hanti,C8\text{-}Hanti}$ = 9.8 Hz, $^3J_{C7\text{-}Hanti,C8\text{-}Hsyn}$ = 4.1 Hz, $^3J_{C7\text{-}Hanti,C1\text{-}H}$ = 2.3 Hz, 1H, C7-H_{anti}), 1.28 (dddd, $^2J_{C8\text{-}Hsyn,C8\text{-}Hanti}$ = 12.3 Hz, $^3J_{C8\text{-}Hsyn,C7\text{-}Hsyn}$ = 12.1 Hz, $^3J_{C8\text{-}Hsyn,C7\text{-}Hanti}$ = 4.1 Hz, $^3J_{C8\text{-}Hsyn,C4\text{-}H}$ = 3.3 Hz, 1H, C8-H_{syn}), 1.20 (ddddd, $^3J_{C7\text{-}Hsyn,C8\text{-}Hsyn}$ = 12.1 Hz, $^2J_{C7\text{-}Hsyn,C7\text{-}Hanti}$ = 11.8 Hz, $^3J_{C7\text{-}Hsyn,C8\text{-}Hanti}$ = 3.9 Hz, $^3J_{C7\text{-}Hsyn,C1\text{-}H}$ = 3.1 Hz, $^4J_{C7\text{-}Hsyn,C6\text{-}Hendo}$ = 3.0 Hz, 1H, C7-H_{syn}), 0.84 (dddd, $^2J_{C6\text{-}Hendo,C6\text{-}Hexo}$ = 12.5 Hz, $^3J_{C6\text{-}Hendo,C5\text{-}H}$ = 4.7 Hz, $^3J_{C6\text{-}Hendo,C1\text{-}H}$ = 3.0 Hz, $^4J_{C6\text{-}Hendo,C7\text{-}Hsyn}$ = 3.0 Hz, 1H, C6-H_{endo}) ppm.

^{13}C NMR (150 MHz, $CDCl_3$): δ = 179.6 (C10), 135.3 (C2), 131.6 (C3), 41.9 (C9), 34.4 (C4), 34.3 (C5), 33.8 (C6), 30.0 (C1), 26.1 (C8), 24.3 (C7) ppm.

IR (ATR): $\tilde{\nu}$ = 3042 (w), 2935 (m), 2864 (vw), 1702 (vs), 1408 (w), 1376 (vw), 1294 (w), 1230 (w), 1196 (vw), 1163 (vw), 1093 (vw), 938 (w), 833 (vw), 706 (m) cm^{-1}.

HRMS (EI): m/z for $C_{10}H_{14}O_2^+$ $[M]^+$: calcd.: 166.0988
found: 166.0990.

Iodolactonization of Carboxylic Acid 248



Carboxylic acid **248** (16.1 g, 97.0 mmol, 1.00 eq.) was suspended in H_2O (47.0 mL) and dissolved by dropwise addition of cold 50 wt-% aqueous NaOH. Solid $NaHCO_3$ was added to saturation and a solution of I_2 (40.9 g, 161 mmol, 1.66 eq.) and KI (37.5 g, 226 mmol, 2.33 eq.) in H_2O (125 mL) was added. The resulting mixture was stirred at room temperature for 2 h and then decolorized by addition of solid $Na_2S_2O_3$. The layers were separated and the aqueous layer was extracted with EtOAc (3 x 600 mL). The combined organic layer was washed with 1 M NaOH (450 mL), brine (450 mL), dried (Na_2SO_4) and concentrated *in vacuo*. The desired iodolactone **249** (25.9 g, 91%) was obtained as a colorless solid by recrystallization from EtOAc. Purification of the residue after four recrystallizations by flash column chromatography (4 x 21 cm, silica, hexanes : EtOAc = 9 : 1 to 4 : 1, 20 mL) afforded rearranged iodolactone **481** (#23–28, 122 mg, 0.4%) as a colorless solid. Crystals suitable for single crystal X-ray diffraction were obtained by recrystallization from EtOAc for both compounds.

*2-Iodo-4-oxatricyclo[5.3.1.0^{3,8}]undecan-5-one (**249**)*

$C_{10}H_{13}IO_2$ M_r = 292.12 g·mol^{-1}.

TLC R_f = 0.39 (hexanes : EtOAc = 3 : 1).

mp 125 – 127 °C.

^{1}H NMR (600 MHz, $CDCl_3$): δ = 5.03 – 5.00 (m, 1H, C3-H), 4.32 – 4.27 (m, 1H, C2-H), 2.58 (dd, $^2J_{C5\text{-}Ha,C5\text{-}Hb}$ = 18.2 Hz, $^2J_{C5\text{-}Ha,C6\text{-}H}$ = 5.4 Hz, 1H, C5-H_A*), 2.48 (dd, $^2J_{C5\text{-}Hb,C5\text{-}Ha}$ = 18.2 Hz, $^3J_{C5\text{-}Hb,C6\text{-}H}$ = 1.9 Hz, 1H, C5-H_B*), 2.20 (ddd, $^2J_{C10\text{-}Hanti,C10\text{-}Hsyn}$ = 14.1 Hz, $^3J_{C10\text{-}Hanti,C6\text{-}H}$ = 11.1 Hz, $^3J_{C10\text{-}Hanti,C1\text{-}H}$ = 3.7 Hz, 1H, C10-H_{anti}), 2.15 – 2.08 (m, 1H, C6-H), 2.01 – 1.93 (m, 2H, C1-H, C9-H_{endo}**), 1.89 – 1.84 (m, 1H, C7-H), 1.82 – 1.74 (m, 2H, C8-H), 1.54 – 1.45 (m, 1H, C9-H_{exo}**), 1.39 (dddd, $^2J_{C10\text{-}Hsyn,C10\text{-}Hanti}$ = 14.1 Hz, $^3J_{C10\text{-}Hsyn,C6\text{-}H}$ = 5.1 Hz, $^3J_{C10\text{-}Hsyn,C1\text{-}H}$ = 2.8 Hz, $^4J_{C10\text{-}Hsyn,C9\text{-}Hendo}$ = 2.8 Hz, 1H, C10-H_{syn}) ppm.

^{13}C NMR (150 MHz, $CDCl_3$): δ = 168.9 (C4), 87.1 (C3), 39.3 (C5), 33.7 (C10), 33.2 (C2), 32.3 (C1), 29.8 (C7), 24.5 (C6), 21.4 (C9), 20.0 (C8) ppm.

IR (ATR): $\tilde{\nu}$ = 3425 (vw), 2943 (w), 2903 (vw), 2866 (vw), 1718 (vs), 1462 (vw), 1454 (vw), 1439 (vw), 1410 (vw), 1381 (w), 1370 (w), 1353 (m), 1274 (vw), 1244 (vw), 1225 (w), 1210 (w), 1179 (m), 1143 (w), 1094 (w), 1056 (m), 1032 (m), 1004 (m),

968 (vw), 953 (vw), 878 (vw), 854 (vw), 836 (w), 814 (vw), 792 (vw), 740 (vw), 674 (vw) cm^{-1}.

HRMS (EI): m/z for $C_{10}H_{13}IO_2^+$ $[M]^+$: calcd.: 291.9955
found: 291.9940.

*6-Iodo-4-oxatricyclo[7.1.1.0^{5,10}]undecan-3-one (**481**)*

$C_{10}H_{13}IO_2$ M_r = 292.12 g·mol^{-1}.

TLC R_f = 0.44 (hexanes : EtOAc = 3 : 1).

mp 94 – 97°C.

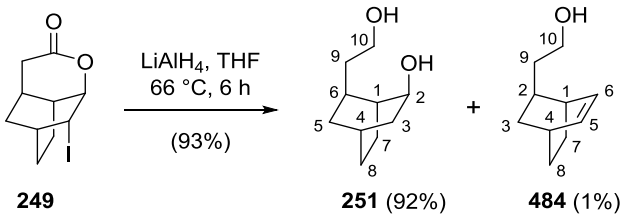
^{1}H NMR (600 MHz, $CDCl_3$): δ = 4.79 (dd, $^3J_{C4\text{-}H,C9\text{-}H}$ = 5.6 Hz, $^3J_{C4\text{-}H,C5\text{-}H}$ = 3.3 Hz, 1H, C4-H), 4.56 (ddd, $^3J_{C5\text{-}H,C4\text{-}H}$ = 3.3 Hz, $^3J_{C5\text{-}H,C6\text{-}Ha}$ = 3.3 Hz, $^3J_{C5\text{-}H,C6\text{-}Hb}$ = 3.3 Hz, 1H, C5-H), 2.97 – 2.87 (m, 2H, C1-H, C9-H), 2.60 – 2.52 (m, 1H, C8-H), 2.48 (dd, $^2J_{C2\text{-}Ha,C2\text{-}Hb}$ = 16.8 Hz, $^3J_{C2\text{-}Ha,C1\text{-}H}$ = 2.5 Hz, 1H, C2-H_A), 2.38 (dd, $^2J_{C2\text{-}Hb,C2\text{-}Ha}$ = 16.8 Hz, $^3J_{C2\text{-}Hb,C1\text{-}H}$ = 4.0 Hz, 1H, C2-H_B), 2.10 – 2.05 (m, 1H, C10-H_A), 2.02 (dddd, $^2J_{C6\text{-}Ha,C6\text{-}Hb}$ = 15.3 Hz, $^3J_{C6\text{-}Ha,C7\text{-}Ha}$ = 12.4 Hz, $^3J_{C6\text{-}Ha,C7\text{-}Hb}$ = 4.7 Hz, $^3J_{C6\text{-}Ha,C5\text{-}H}$ = 3.3 Hz, 1H, C6-H_A), 1.85 (dddd, $^2J_{C7\text{-}Ha,C7\text{-}Hb}$ = 14.6 Hz, $^3J_{C7\text{-}Ha,C6\text{-}Ha}$ = 12.4 Hz, $^3J_{C7\text{-}Ha,C6\text{-}Hb}$ = 6.9 Hz, $^3J_{C7\text{-}Ha,C8\text{-}H}$ = 5.1 Hz, 1H, C7-H_A), 1.74 – 1.67 (m, 1H, C6-H_B), 1.62 – 1.55 (m, 1H, C10-H_B), 1.45 – 1.39 (m, 1H, C7-H_B) ppm.

^{13}C NMR (150 MHz, $CDCl_3$): δ = 171.5 (C3), 78.2 (C4), 32.9 (C2), 30.2 (C10), 30.0 (C9), 28.2 (C1), 27.7 (C5), 27.1 (C8), 23.0 (C6), 22.4 (C7) ppm.

IR (ATR): $\tilde{\nu}$ = 2973 (vw), 2948 (vw), 2927 (w), 2847 (vw), 1735 (vs), 1443 (vw), 1427 (vw), 1361 (w), 1325 (vw), 1299 (vw), 1283 (vw), 1267 (vw), 1249 (vw), 1236 (w), 1228 (m), 1215 (w), 1174 (w), 1146 (w), 1094 (vw), 1066 (w), 1037 (m), 973 (s), 943 (vw), 878 (vw), 851 (vw), 838 (vw), 791 (vw), 756 (vw), 729 (vw), 659 (vw) cm^{-1}.

HRMS (EI): m/z for $C_{10}H_{13}IO_2^+$ $[M]^+$: calcd.: 291.9955
found: 291.9956.

Reduction of Iodolactone 249



249 **251** (92%) **484** (1%)

A suspension of $LiAlH_4$ (9.96 g, 263 mmol, 5.00 eq.) in THF (400 mL) was heated to 66 °C and a solution of iodolactone **249** (15.3 g, 52.5 mmol, 1.00 eq.) in THF (100 mL) was added over the course of 1.5 h. After complete addition the reaction mixture was refluxed for an additional 6 h and was then cooled to 0 °C. Rochelle salt was added to provide a homogeneous solution. The reaction mixture was

extracted with EtOAc (3 x 400 mL). The combined organic layer was washed with brine (350 mL), dried (Na_2SO_4) and concentrated *in vacuo*. Purification of the residue by flash column chromatography (4 x 21 cm, silica, hexanes : EtOAc = 1 : 1, 20 mL) afforded unsaturated alcohol **484** (#15–16, 13 mg, 1%) as a colorless oil and desired diol **251** (#65–90, 8.26 g, 92%) as a colorless solid. Recrystallization of diol **251** from CH_2Cl_2 afforded crystals suitable for single crystal X-ray diffraction.

*2-endo-Hydroxy-6-endo-(2-hydroxyethyl)-bicyclo[2.2.2]octane (**251**)*

$C_{10}H_{18}O_2$ M_r = 170.25 g·mol^{-1}.

TLC R_f = 0.21 (hexanes : EtOAc = 1 : 1).

mp 81 – 83 °C.

^{1}H NMR (600 MHz, $CDCl_3$): δ = 4.02 (dddd, $^3J_{C2\text{-}H,C3\text{-}Hanti}$ = 9.8 Hz, $^3J_{C2\text{-}H,C3\text{-}Hsyn}$ = 3.5 Hz, $^3J_{C2\text{-}H,C1\text{-}H}$ = 3.5 Hz, $^3J_{C2\text{-}H,C6\text{-}H}$ = 1.4 Hz, 1H, C2-H), 3.73 (ddd, $^2J_{C10\text{-}H_A,C10\text{-}H_B}$ = 10.8 Hz, $^3J_{C10\text{-}H_A,C9\text{-}H_A}$ = 5.5 Hz, $^3J_{C10\text{-}H_A,C9\text{-}H_B}$ = 5.5 Hz, 1H, C10-H_A), 3.64 (ddd, $^2J_{C10\text{-}H_B,C10\text{-}H_A}$ = 10.8 Hz, $^3J_{C10\text{-}H_B,C9\text{-}H_A}$ = 8.1 Hz, $^3J_{C10\text{-}H_B,C9\text{-}H_B}$ = 5.2 Hz, 1H, C10-H_B), 2.39 (br s, 2H, C2-OH, C10-OH), 1.98 (dddd, $^2J_{C3\text{-}Hexo,C3\text{-}Hendo}$ = 13.2 Hz, $^3J_{C3\text{-}Hexo,C2\text{-}H}$ = 9.8 Hz, $^3J_{C3\text{-}Hexo,C4\text{-}H}$ = 3.0 Hz, $^4J_{C3\text{-}Hexo,C5\text{-}Hexo}$ = 2.5 Hz, 1H, C3-H_{exo}), 1.92 (dddd, $^2J_{C9\text{-}H_A,C9\text{-}H_B}$ = 13.8 Hz, $^3J_{C9\text{-}H_A,C10\text{-}H_B}$ = 8.1 Hz, $^3J_{C9\text{-}H_A,C6\text{-}H}$ = 8.0 Hz, $^3J_{C9\text{-}H_A,C10\text{-}H_A}$ = 5.5 Hz, 1H, C9-H_A), 1.86 – 1.78 (m, 3H, C1-H, C5-H_{endo}, C9-H_B), 1.78 – 1.72 (m, 1H, C6-H), 1.72 – 1.68 (m, 1H, C4-H), (m, 1H, C7-H_{anti}), 1.46 – 1.37 (m, 3H, C3-H_{endo}, C7-H_{syn}, C8-H_{anti}), 1.37 – 1.30 (m, 1H, C8-H_{syn}), 1.24 (dddd, $^2J_{C5\text{-}Hexo,C5\text{-}Hendo}$ = 12.2 Hz, $^3J_{C5\text{-}Hexo,C6\text{-}H}$ = 5.9 Hz, $^3J_{C5\text{-}Hexo,C4\text{-}H}$ = 2.5 Hz, $^4J_{C5\text{-}Hexo,C3\text{-}H_A}$ = 2.5 Hz, 1H, C5-H_{exo}) ppm.

^{13}C NMR (150 MHz, $CDCl_3$): δ = 71.3 (C2), 62.2 (C10), 40.6 (C9), 38.2 (C3), 34.9 (C1), 34.7 (C5), 33.1 (C6), 25.9 (C7), 25.5 (C4), 23.6 (C8) ppm.

IR (ATR): $\tilde{\nu}$ = 3324 (m), 2925 (vs), 2861 (s), 1653 (vw), 1453 (m), 1378 (w), 1331 (w), 1163 (w), 1102 (m), 1078 (m), 1035 (vs), 1002 (s), 948 (w), 928 (w), 874 (w), 846 (w), 752 (m) cm^{-1}.

HRMS (EI): m/z for $C_{10}H_{18}O_2^+$ $[M]^+$: calcd.: 170.1301
found: 170.1211.

*2-endo-Hydroxyethylbicyclo[2.2.2]oct-5-ene (**484**)*

$C_{10}H_{16}O$ M_r = 152.23 g·mol^{-1}.

TLC R_f = 0.76 (hexanes : EtOAc = 1 : 1).

^{1}H NMR (600 MHz, $CDCl_3$): δ = 6.25 (ddd, $^3J_{C2\text{-}H,C3\text{-}H}$ = 8.0 Hz, $^3J_{C2\text{-}H,C1\text{-}H}$ = 6.6 Hz, $^4J_{C2\text{-}H,C4\text{-}H}$ = 1.2 Hz, 1H, C2-H), 6.14 – 6.10 (m, 1H, C3-H), 3.65 – 3.58 (m, 2H, C10-H), 2.49 – 2.44 (m, 1H, C1-H), 2.41 – 2.36 (m, 1H, C4-H), 1.80 – 1.72 (m, 2H, C5-H, C6-H_{exo}), 1.54 – 1.40 (m, 3H, C7-H_{syn}, C8-H_{syn}, C9-H_A), 1.30 – 1.17 (m, 4H,

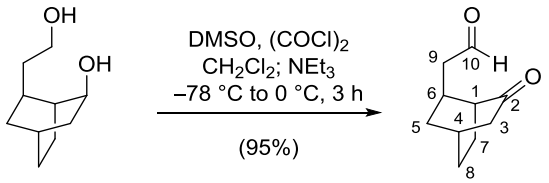
C7-H_{anti}, C8-H_{anti}, C9-H_B, OH), 0.82 (dddd, $^2J_{C6\text{-}Hendo,C6\text{-}Hexo}$ = 11.7 Hz, $^3J_{C6\text{-}Hendo,C1\text{-}H}$ = 7.3 Hz, $^3J_{C6\text{-}Hendo,C5\text{-}H}$ = 4.3 Hz, $^4J_{C6\text{-}Hendo,C7\text{-}Hendo}$ = 3.1 Hz, 1H, C6-H_{endo}) ppm.

^{13}C NMR (150 MHz, $CDCl_3$): δ = 134.7 (C2), 132.1 (C3), 61.2 (C10), 40.8 (C9), 34.7 (C4), 34.2 (C6), 34.2 (C5), 30.2 (C1), 26.5 (C8), 24.6 (C7) ppm.

IR (ATR): $\tilde{\nu}$ = 3312 (br w), 3039 (vw), 2929 (s), 2861 (m), 1637 (vw), 1614 (vw), 1463 (vw), 1450 (vw), 1430 (vw), 1375 (w), 1312 (vw), 1290 (vw), 1272 (vw), 1228 (vw), 1209 (vw), 1177 (vw), 1162 (vw), 1108 (vw), 1070 (w), 1050 (s), 1040 (m), 993 (w), 946 (vw), 937 (vw), 920 (vw), 897 (vw), 856 (vw), 814 (vw), 799 (vw), 701 (vs), 656 (w) cm^{-1}.

HRMS (EI): m/z for $C_{10}H_{16}O^+$ $[M]^+$: calcd.: 152.1196
found: 152.1203.

2-(2-oxobicyclo[2.2.2]octan-6-*endo*-yl)acetaldehyde (478)



251 **478**

A solution of DMSO (2.30 mL, 2.53 g, 32.4 mmol, 5.40 eq.) in CH_2Cl_2 (16.6 mL) was added dropwise to a solution of oxalyl chloride (7.80 mL, 2 m in CH_2Cl_2, 10.4 g, 15.6 mmol, 2.60 eq.) in CH_2Cl_2 (58.0 mL) at –78 °C. The internal temperature was monitored during the addition to insure that the temperature did not rise above –50 °C. At –78 °C a solution of diol **251** (1.02 g, 6.00 mmol, 1.00 eq.) in CH_2Cl_2 (20.0 mL) was added dropwise to the dimethylchlorosulfonium chloride solution and after complete addition the mixture was stirred for an additional 1 h at –78 °C. During the addition of the alcohol precipitation of a white solid was observed to afford an opaque solution. Triethylamine (8.34 mL, 60.0 mmol, 10.0 eq.) was added in one portion and the reaction was stirred for 10 min at –78 °C during which time the precipitate dissolved again to afford a clear solution. The solution was slowly (30 min) warmed to 0 °C and maintained at 0 °C for 1 h. Upon warming a white solid again precipitated. The cold solution was partitioned between saturated aqueous $NaHCO_3$ (100 mL) and CH_2Cl_2 (50 mL). The layers were separated, and the aqueous layer was extracted with CH_2Cl_2 (3 x 100 mL). The combined organic layer was washed with brine (100 mL), dried (Na_2SO_4) and concentrated *in vacuo*. The crude reaction products (0.95 g, 95%) were used without further purification in the next step.

$C_{10}H_{14}O_2$ M_r = 166.22 g·mol^{-1}.

TLC R_f = 0.51 (hexanes : EtOAc = 1 : 1).

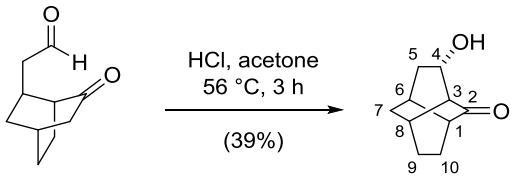
^{1}H NMR (600 MHz, $CDCl_3$): δ = 9.72 – 9.70 (dd, $^3J_{C10\text{-}H,C9\text{-}H_B}$ = 1.5 Hz, $^3J_{C10\text{-}H,C9\text{-}H_A}$ = 1.3 Hz, 1H, C10-H), 2.54 (ddddd, $^3J_{C6\text{-}H,C5\text{-}Hexo}$ = 10.4 Hz, $^3J_{C6\text{-}H,C9\text{-}H_B}$ = 8.3 Hz, $^3J_{C6\text{-}H,C9\text{-}H_A}$ = 6.2 Hz, $^3J_{C6\text{-}H,C5\text{-}Hendo}$ = 6.1 Hz, $^3J_{C6\text{-}H,C1\text{-}H}$ = 2.3 Hz, 1H, C6-H), 2.45 (ddd, $^2J_{C9\text{-}H_A,C9\text{-}H_B}$ = 17.7 Hz, $^3J_{C9\text{-}H_A,C6\text{-}H}$ = 6.2 Hz, $^3J_{C9\text{-}H_A,C10\text{-}H}$ = 1.3 Hz, 1H, C9-H_A), 2.30 (ddd, $^2J_{C9\text{-}H_B,C9\text{-}H_A}$ = 17.7 Hz, $^3J_{C9\text{-}H_B,C6\text{-}H}$ = 8.3 Hz, $^3J_{C9\text{-}H_A,C10\text{-}H}$ = 1.5 Hz, 1H, C9-H_B), 2.27 – 2.22 (m, 1H, C3-H_{endo}*), 2.20 – 2.07 (m, 4H, C1-H, C3-H_{exo}*, C4-H, C5-H_{exo}), 1.93 – 1.85 (m, 1H, C7-H_{anti}), 1.81 (dddd, $^2J_{C7\text{-}Hsyn,C7\text{-}Hanti}$ = 14.0 Hz, $^3J_{C7\text{-}Hsyn,C8\text{-}Hsyn}$ = 11.3 Hz, $^3J_{C7\text{-}Hsyn,C8\text{-}Hanti}$ = 5.7 Hz, $^3J_{C7\text{-}Hsyn,C1\text{-}H}$ = 2.8 Hz, 1H, C7-H_{syn}), 1.72 – 1.59 (m, 2H, C8-H), 1.08 (dddd, $^2J_{C5\text{-}Hendo,C5\text{-}Hexo}$ = 11.4 Hz, $^3J_{C5\text{-}Hendo,C6\text{-}H}$ = 5.8 Hz, $^3J_{C5\text{-}Hendo,C4\text{-}H}$ = 2.6 Hz, $^4J_{C5\text{-}Hendo,C8\text{-}Hsyn}$ = 2.8 Hz, 1H, C5-H_{endo}) ppm.

^{13}C NMR (150 MHz, $CDCl_3$): δ = 216.5 (C2), 200.7 (C10), 51.3 (C9), 47.5 (C1), 45.0 (C3), 33.4 (C5), 30.5 (C6), 28.0 (C4), 23.5 (C8), 23.1 (C7) ppm.

IR (ATR): $\tilde{\nu}$ = 3422 (vw), 2937 (w), 2870 (w), 2726 (vw), 1716 (vs), 1454 (vw), 1402 (w), 1330 (vw), 1288 (vw), 1226 (vw), 1159 (vw), 1130 (vw), 1102 (w), 1067 (vw), 1052 (vw), 956 (vw), 903 (vw), 743 (vw), 678 (vw), 614 (vw), 610 (vw) cm^{-1}.

HRMS (EI): m/z for $C_{10}H_{14}O_2^+$ $[M]^+$: calcd.: 166.0988
found: 166.0986.

4-*endo*-Hydroxytricyclo[4.4.0.0^{3,8}]decan-2-one (*endo*-471)



478 ***endo*-471**

To a solution of keto aldehyde **478** (997 mg, 6.00 mmol, 1.00 eq.) in acetone (25.6 mL) was added 1 M HCl (2.40 mL, 2.40 mmol, 0.400 eq.) and the resulting solution was heated to reflux for 3 h. After cooling to 0 °C, $NaHCO_3$ (201 mg, 2.40 mmol, 0.400 eq.) and water (30 mL) were added and the acetone was removed *in vacuo*. The residue was extracted with EtOAc (3 x 50 mL) and the combined organic layer was dried (Na_2SO_4) and concentrated *in vacuo*. Purification of the residue by flash column chromatography (5 x 14 cm, silica, hexanes : EtOAc = 3 : 1 -> 3 : 2 -> 1 : 1, 100 mL, #36–50) afforded hydroxytwistanone ***endo*-471** (389 mg, 39%) as a colorless waxy amorphous solid. Significant amounts of starting material (590 mg, 3.55 mmol, ~55%) could be reisolated and used for another cycle of the aldol reaction.

$C_{10}H_{14}O_2$ M_r = 166.22 g·mol^{-1}.

TLC R_f = 0.17 (hexanes : EtOAc = 1 : 1).

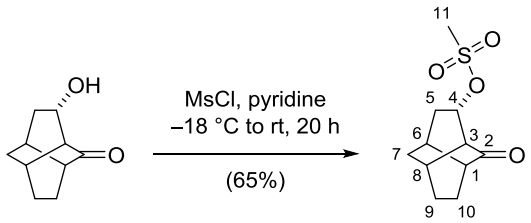
^{1}H NMR (600 MHz, $CDCl_3$): δ = 4.29 (ddd, $^3J_{C4\text{-}H,C5\text{-}H_A}$ = 8.0 Hz, $^3J_{C4\text{-}H,C5\text{-}H_B}$ = 8.0 Hz, $^3J_{C4\text{-}H,C3\text{-}H}$ = 2.0 Hz, 1H, C4-H), 2.36 – 2.21 (m, 5H, C1-H, C3-H, C5-H_A, C6-H, C8-H), 1.95 – 1.87 (m, 1H, C10-H_A), 1.85 – 1.78 (m, 1H, C10-H_B), 1.71 (br s, 1H, O-H), 1.65 – 1.58 (m, 1H, C9-H_A), 1.58 – 1.51 (m, 1H, C7-H_A), 1.51 – 1.45 (m, 2H, C7-H_B, C9-H_B), 1.22 – 1.16 (m, 1H, C5-H_B) ppm.

^{13}C NMR (150 MHz, $CDCl_3$): δ = 221.0 (C2), 70.2 (C4), 57.2 (C3), 48.5 (C1), 37.7 (C5), 31.6 (C6), 31.0 (C8), 25.7 (C9), 25.5 (C7), 24.5 (C10) ppm.

IR (ATR): $\tilde{\nu}$ = 3397 (w), 2937 (m), 2863 (w), 1725 (vs), 1666 (vw), 1478 (vw), 1447 (vw), 1325 (w), 1309 (vw), 1267 (w), 1205 (vw), 1146 (vw), 1129 (w), 1091 (m), 1071 (m), 1052 (w), 1040 (w), 1027 (w), 1005 (w), 978 (w), 944 (vw), 925 (vw), 869 (vw), 858 (vw), 832 (vw), 806 (vw), 780 (vw), 728 (w), 700 (vw), 682 (vw) cm^{-1}.

HRMS (EI): m/z for $C_{10}H_{14}O_2^+$ $[M]^+$: calcd.: 166.0988
found: 166.0990.

4-*endo*-Mesyloxytricyclo[4.4.0.0^{3,8}]decan-2-one (485)



***endo*-471** **485**

To a solution of ketoalcohol ***endo*-471** (201 mg, 1.21 mmol, 1.00 eq.) in pyridine (10.1 mL) at –18 °C was added methanesulfonyl chloride (0.258 mL, 383 mg, 3.34 mmol, 2.76 eq.). The resulting solution was stirred at room temperature for 20 h and was then diluted with $CHCl_3$ (75 mL). The organic layer was washed with 10% aqueous $CuSO_4$ (5 x 40 mL), brine (100 mL), dried (Na_2SO_4) and concentrated *in vacuo*. Purification of the residue by flash column chromatography (3 x 22 cm, silica, hexanes : EtOAc = 3 : 1 to 1 : 1, 20 mL, #77–100) afforded keto mesylate **485** (193 mg, 65%) as a colorless solid. Recrystallization from EtOAc afforded crystals suitable for single crystal X-ray diffraction.

$C_{11}H_{16}O_4S$ M_r = 244.31 g·mol^{-1}.

TLC R_f = 0.21 (hexanes : EtOAc = 1 : 1).

mp 128 – 130 °C.

^{1}H NMR (600 MHz, $CDCl_3$): δ = 5.22 – 5.15 (m, 1H, C4-H), 3.06 (s, 3H, C11-H), 2.62 (dddd, $^3J_{C3\text{-}H,C8\text{-}H}$ = 6.1 Hz, $^3J_{C3\text{-}H,C4\text{-}H}$ = 2.2 Hz, $^4J_{C3\text{-}H,C1\text{-}H}$ = 1.2 Hz, $^4J_{C3\text{-}H,C7\text{-}Hendo}$ = 1.2 Hz, 1H, C3-H), 2.44 – 2.38 (m, 2H, C1-H, C8-H), 2.39 – 2.31 (m, 2H, C5-H_A), 1.92 (dddd,

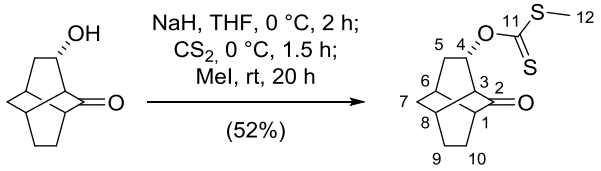
$^2J_{C10\text{-}H_A,C10\text{-}H_B}$ = 13.0 Hz, $^3J_{C10\text{-}H_A,C9\text{-}H_A}$ = 10.0 Hz, $^3J_{C10\text{-}H_A,C9\text{-}H_B}$ = 9.3 Hz, $^3J_{C10\text{-}H_A,C1\text{-}H}$ = 1.8 Hz, 1H, C10-H_A), 1.85 (dddd, $^2J_{C10\text{-}H_B,C10\text{-}H_A}$ = 13.0 Hz, $^3J_{C10\text{-}H_B,C9\text{-}H_B}$ = 8.7 Hz, $^3J_{C10\text{-}H_B,C10\text{-}H_A}$ = 4.4 Hz, $^3J_{C10\text{-}H_B,C1\text{-}H}$ = 0.9 Hz, 1H, C10-H_B), 1.66 – 1.48 (m, 5H, C5-H_B, C7-H, C9-H) ppm.

^{13}C NMR (150 MHz, $CDCl_3$): δ = 217.3 (C2), 77.8 (C4), 53.1 (C3), 47.8 (C1), 39.3 (C11), 34.8 (C5), 31.1 (C8), 30.9 (C6), 25.2 (C7), 25.0 (C9), 24.8 (C10) ppm.

IR (ATR): $\tilde{\nu}$ = 3421 (vw), 3176 (vw), 2937 (m), 2869 (w), 2655 (vw), 1722 (vs), 1455 (vw), 1389 (w), 1357 (w), 1331 (vw), 1304 (vw), 1225 (w), 1182 (w), 1162 (w), 1100 (w), 1088 (vw), 1055 (w), 1012 (w), 970 (vw), 953 (vw), 914 (vw), 898 (vw), 838 (vw), 745 (vw) cm^{-1}.

HRMS (EI): m/z for $C_{11}H_{16}O_4S^+$ $[M]^+$: calcd.: 244.0764
found: 244.0759.

_S_-Methyl-_O_-(2-oxotricyclo[4.4.0.0^{3,8}]decan-4-yl) carbonodithioate (486)



***endo*-471** **486**

To a solution of ketoalcohol ***endo*-471** (50.0 mg, 0.300 mmol, 1.00 eq.) in THF (24.0 mL) at 0 °C was added sodium hydride (72.0 mg, 3.00 mmol, 10.0 eq.). The resulting reaction mixture was stirred at 0 °C for 2 h after which time CS_2 (1.20 mL, 1.51 g, 19.8 mmol, 66.0 eq.) was added and the mixture was stirred at 0 °C for an additional 1.5 h. Methyl iodide (0.600 mL, 1.37 g, 9.64 mmol, 32.1 eq.) was added and the solution was allowed to warm to room temperature and stirred at room temperature for 20 h. To the reaction mixture were added successively Et_2O (25 mL) and ice water (12 mL). The aqueous layer was extracted with Et_2O (3 x 20 mL) and the combined organic layer was washed with brine (50 mL), dried (Na_2SO_4) and concentrated *in vacuo*. Purification of the residue by flash column chromatography (2 x 15 cm, silica, hexanes : EtOAc = 9 : 1, 20 mL, #27–37) afforded the desired xanthate **486** (40 mg, 52%) as a yellow oil.

$C_{12}H_{16}O_2S_2$ M_r = 256.39 g·mol^{-1}.

TLC R_f = 0.17 (hexanes : EtOAc = 9 : 1).

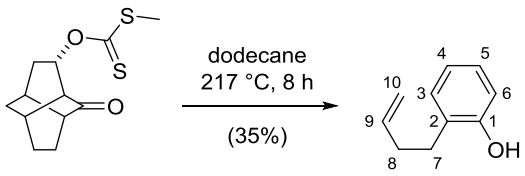
^{1}H NMR (300 MHz, $CDCl_3$): δ = 5.98 – 5.90 (m, 1H, C4-H), 2.65 – 2.58 (m, 1H, C3-H), 2.50 (s, 3H, C12-H), 2.46 – 2.32 (m, 4H, C1-H, C5-H_A, C6-H, C8-H), 1.99 – 1.77 (m, 2H, C9-H*), 1.68 – 1.42 (m, 5H, C5-H_B, C7-H, C10-H*) ppm.

^{13}C NMR (75 MHz, $CDCl_3$): δ = 218.5 (C11), 214.8 (C2), 80.4 (C4), 52.5 (C3), 48.0 (C1), 33.6 (C5), 31.0 (C6), 31.0 (C8), 25.6 (C7*), 25.2 (C9*), 25.0 (C10*), 18.8 (C12) ppm.

IR (ATR): $\tilde{\nu}$ = 2936 (w), 2883 (vw), 2865 (vw), 1735 (vs), 1480 (vw), 1459 (vw), 1446 (vw), 1422 (vw), 1323 (vw), 1302 (vw), 1273 (w), 1239 (m), 1224 (s), 1197 (vs), 1163 (w), 1146 (w), 1128 (m), 1095 (w), 1071 (vs), 1054 (vs), 1046 (vs), 1031 (s), 1020 (m), 993 (vw), 967 (w), 951 (w), 928 (vw), 874 (vs), 858 (vw), 833 (vw), 807 (vw), 781 (vw), 740 (vw), 724 (vw) cm^{-1}.

HRMS (EI): m/z for $C_{12}H_{16}O_2S_2^+$ $[M]^+$: calcd.: 256.0586
found: 256.0589.

2-(But-3-en-1-yl)phenol (487)



486 **487**

Xanthate **486** (39.5 mg, 0.154 mmol, 1.00 eq.) was dissolved in dodecane (15.0 mL) and the solution was heated to 217 °C for 8 h. The reaction mixture was allowed to cool to room temperature and was directly purified by flash column chromatography (3 x 23 cm, silica, *n*-pentane : Et_2O = 9 : 1, 20 mL, #23–28) to afford only retro-Diels-Alder product **39** (8 mg, 35%) and starting material **37**. Due to the volatility of the compound no complete separation from the solvent was possible.

$C_{10}H_{12}O$ M_r = 148.20 $g \cdot mol^{-1}$.

TLC R_f = 0.34 (hexanes : EtOAc = 9 : 1).

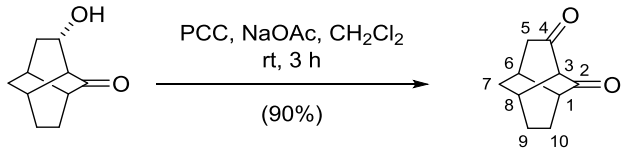
^{1}H NMR (300 MHz, $CDCl_3$): δ = 7.15 – 7.10 (m, 1H, C3-H), 7.09 – 7.05 (m, 1H, C5-H), 6.90 – 6.84 (m, 1H, C4-H), 6.78 – 6.74 (m, 1H, C6-H), 5.98 – 5.83 (m, 1H, C9-H), 5.12 – 4.97 (m, 2H, C10-H), 4.95 (s, 1H, OH), 2.76 – 2.68 (m, 2H, C7-H), 2.44 – 2.33 (m, 2H, C8-H) ppm.

^{13}C NMR (75 MHz, $CDCl_3$): δ = 153.7 (C1), 138.4 (C9), 130.4 (C3), 128.0 (C2), 127.3 (C5), 120.9 (C4), 115.4 (C6), 115.2 (C10), 34.0 (C8), 29.8 (C7) ppm.

IR (ATR): $\tilde{\nu}$ = 3019 (vw), 2925 (vw), 2849 (vw), 1711 (m), 1417 (vw), 1362 (w), 1218 (w), 1090 (vw), 752 (vs), 667 (w) cm^{-1}.

HRMS (EI): m/z for $C_{10}H_{12}O^+$ $[M]^+$: calcd.: 148.0883
found: 148.0887.

Tricyclo[4.4.0.0^{3,8}]decan-2,4-dione (488)



***endo*-471** **488**

A mixture of PCC (73.6 g, 342 mmol, 5.00 eq.), sodium acetate (29.4 g, 359 mmol, 5.25 eq.), 4 Å molecular sieves (20 g) and celite (150 g) was dried under high vacuum at room temperature for 1 h. The solids were suspended in CH_2Cl_2 (400 mL) and to the stirred mixture was added a solution of ketoalcohol ***endo*-471** (11.4 g, 68.3 mmol, 1.00 eq.) in CH_2Cl_2 (500 mL). The resulting mixture was stirred for 3 h at room temperature and was then filtered over a short silica column. The residue was washed with CH_2Cl_2 (2 L) and the combined filtrate was concentrated *in vacuo*. A second filtration over a silica column gave diketone **488** (10.1 g, 90%) as a colorless solid.

$C_{10}H_{12}O_2$ M_r = 164.20 g·mol^{-1}.

TLC R_f = 0.30 (hexanes : EtOAc = 3 : 1).

mp 198 – 201 °C.

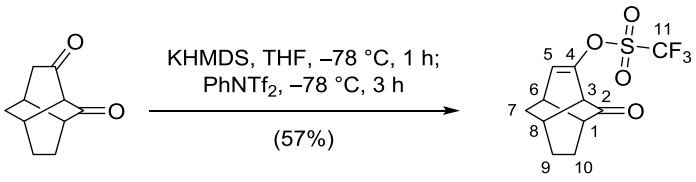
^{1}H NMR (600 MHz, $CDCl_3$): δ = 3.15 (d, $^3J_{C3\text{-}H,C8\text{-}H}$ = 5.9 Hz, 1H, C3-H), 2.66 – 2.61 (m, 1H, C6-H), 2.57 (dd, $^3J_{C1\text{-}H,C6\text{-}H}$ = 4.9 Hz, $^3J_{C1\text{-}H,C10\text{-}Hsyn}$ = 4.9 Hz, 1H, C1-H), 2.55 – 2.51 (m, 1H, C8-H), 2.31 (dd, $^2J_{C5\text{-}Hexo,C5\text{-}Hendo}$ = 17.4 Hz, $^3J_{C5\text{-}Hexo,C6\text{-}H}$ = 4.2 Hz, 1H, C5-H_{exo}), 2.20 – 2.14 (m, 1H, C5-H_{endo}), 2.10 – 2.03 (m, 1H, C10-H_{anti}), 1.99 (ddd, $^2J_{C10\text{-}Hsyn,C10\text{-}Hanti}$ = 13.2 Hz, $^3J_{C10\text{-}Hsyn,C9\text{-}Hsyn}$ = 9.1 Hz, $^3J_{C10\text{-}Hsyn,C1\text{-}H}$ = 4.9 Hz, 1H, C10-H_{syn}), 1.89 (ddd, $^2J_{C7\text{-}Hexo,C7\text{-}Hendo}$ = 13.0 Hz, $^3J_{C7\text{-}Hexo,C6\text{-}H}$ = 5.9 Hz, $^4J_{C7\text{-}Hexo,C5\text{-}Hendo}$ = 2.8 Hz, 1H, C7-H_{exo}), 1.68 (ddd, $^2J_{C9\text{-}Hanti,C9\text{-}Hsyn}$ = 13.3 Hz, $^3J_{C9\text{-}Hanti,C10\text{-}Hanti}$ = 9.2 Hz, $^3J_{C9\text{-}Hanti,C8\text{-}H}$ = 4.3 Hz, 1H, C9-H_{anti}), 1.62 – 1.55 (m, 1H, C9-H_{syn}), 1.49 (dd, $^2J_{C7\text{-}Hendo,C7\text{-}Hexo}$ = 13.0 Hz, $^3J_{C7\text{-}Hendo,C8\text{-}H}$ = 5.7 Hz, 1H, C7-H_{endo}) ppm.

^{13}C NMR (150 MHz, $CDCl_3$): δ = 212.3 (C2), 206.3 (C4), 69.6 (C3), 45.7 (C1), 45.5 (C5), 33.8 (C8), 29.3 (C6), 28.3 (C7), 26.1 (C10), 24.9 (C9) ppm.

IR (ATR): $\tilde{\nu}$ = 2948 (w), 2871 (vw), 1746 (vs), 1716 (vs), 1477 (vw), 1459 (vw), 1412 (vw), 1374 (vw), 1339 (vw), 1312 (w), 1276 (vw), 1254 (vw), 1218 (vw), 1185 (vw), 1143 (vw), 1116 (w), 1060 (m), 1030 (vw), 1010 (vw), 974 (vw), 940 (vw), 900 (vw), 856 (vw), 833 (vw), 805 (vw), 789 (vw), 764 (vw), 722 (vw) cm^{-1}.

HRMS (EI): m/z for $C_{10}H_{12}O_2^+$ $[M]^+$: calcd.: 164.0832
found: 164.0831.

2-Oxotricyclo[4.4.0.0^{3,8}]dec-4-en-2-yl trifluoromethanesulfonate (489)



488 **489**

A solution of dione **488** (852 mg, 5.19 mmol, 1.00 eq.) in THF (10.0 mL) was added to a solution of KHMDS (1.14 g, 5.71 mmol, 1.10 eq.) in THF (140 mL) at –78 °C. The resulting mixture was stirred at –78 °C for 1 h and was then transferred to a solution of $PhNTf_2$ (2.13 g, 5.97 mmol, 1.15 eq.) in THF (60.0 mL) at –78 °C. The reaction mixture was stirred at –78 °C for an additional 3 h and was then quenched by addition of saturated aqueous $NaHCO_3$ (50 mL). The organic layer was separated and the aqueous layer was extracted with Et_2O (3 x 130 mL). The combined organic layer was washed with 10% aqueous NaOH (260 mL), 1 n HCl (260 mL), brine (2 x 260 mL), dried (Na_2SO_4) and concentrated *in vacuo*. Purification of the residue by flash column chromatography (4 x 16 cm, silica, *n*-pentane : Et_2O = 3 : 1, 20 mL, #24–52) afforded enol triflate **489** (875 mg, 57%) as a colorless oil.

$C_{11}H_{11}F_3O_4S$ M_r = 340.08 g·mol^{-1}.

TLC R_f = 0.12 (hexanes : EtOAc = 9 : 1).

^{1}H NMR (600 MHz, $CDCl_3$): δ = 6.31 (dd, $^3J_{C5\text{-}H,C6\text{-}H}$ = 7.3 Hz, $^4J_{C5\text{-}H,C3\text{-}H}$ = 2.5 Hz, 1H, C5-H), 3.37 – 3.32 (m, 1H, C3-H), 3.09 (dddd, $^3J_{C6\text{-}H,C5\text{-}H}$ = 7.3 Hz, $^3J_{C6\text{-}H,C7\text{-}Hexo}$ = 5.4 Hz, $^3J_{C6\text{-}H,C1\text{-}H}$ = 5.3 Hz, $^3J_{C6\text{-}H,C7\text{-}Hendo}$ = 1.0 Hz, 1H, C6-H), 2.38 – 2.31 (m, 1H, C8-H), 2.11 (dddd, $^3J_{C1\text{-}H,C6\text{-}H}$ = 5.3 Hz, $^3J_{C1\text{-}H,C10\text{-}Hsyn}$ = 3.6 Hz, $^3J_{C1\text{-}H,C10\text{-}Hanti}$ = 2.2 Hz, $^4J_{C1\text{-}H,C7\text{-}Hendo}$ = 1.0 Hz, 1H, C1-H), 1.94 (dd, $^2J_{C7\text{-}Hexo,C7\text{-}Hendo}$ = 12.0 Hz, $^3J_{C7\text{-}Hexo,C6\text{-}H}$ = 5.4 Hz, 1H, C7-H_{exo}), 1.88 – 1.82 (m, 2H, C10-H), 1.72 (dddd, $^2J_{C9\text{-}Hanti,C9\text{-}Hsyn}$ = 13.3 Hz, $^3J_{C9\text{-}Hanti,C10\text{-}Hanti}$ = 6.6 Hz, $^3J_{C9\text{-}Hanti,C10\text{-}Hsyn}$ = 4.5 Hz, $^3J_{C9\text{-}Hanti,C8\text{-}H}$ = 3.3 Hz, 1H, C9-H_{anti}), 1.61 (ddddd, $^2J_{C9\text{-}Hsyn,C9\text{-}Hanti}$ = 13.3 Hz, $^3J_{C9\text{-}Hsyn,C10\text{-}Hsyn}$ = 9.6 Hz, $^3J_{C9\text{-}Hsyn,C10\text{-}Hanti}$ = 9.6 Hz, $^3J_{C9\text{-}Hsyn,C8\text{-}H}$ = 1.7 Hz, $^4J_{C9\text{-}Hsyn,C7\text{-}Hendo}$ = 1.7 Hz, 1H, C9-H_{syn}), 1.33 (ddddd, $^2J_{C7\text{-}Hendo,C7\text{-}Hexo}$ = 12.0 Hz, $^3J_{C7\text{-}Hendo,C8\text{-}H}$ = 6.7 Hz, $^4J_{C7\text{-}Hendo,C9\text{-}Hsyn}$ = 1.8 Hz, $^3J_{C7\text{-}Hendo,C8\text{-}H}$ = 1.0 Hz, $^4J_{C7\text{-}Hendo,C1\text{-}H}$ = 1.0 Hz, 1H, C7-H_{endo}) ppm.

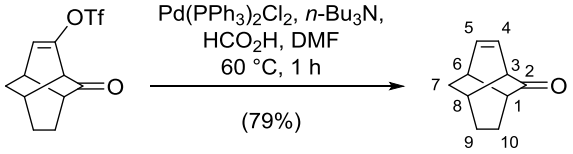
^{13}C NMR (75 MHz, $CDCl_3$): δ = 208.3 (C2), 144.0 (C4), 125.7 (C5), 118.6 (q, $^1J_{C11,C11\text{-}F}$ = 321.1 Hz, C11), 57.5 (C3), 36.6 (C1), 33.3 (C6), 30.8 (C7), 27.7 (C8), 25.1 (C10), 24.4 (C9) ppm.

IR (ATR): $\tilde{\nu}$ = 2959 (vw), 2873 (vw), 1746 (s), 1636 (w), 1479 (vw), 1449 (vw), 1421 (s), 1320 (vw), 1306 (vw), 1276 (vw), 1244 (m), 1205 (vs), 1137 (vs), 1087 (m), 1077 (s), 1049 (s), 1009 (vw), 965 (w), 928 (vw), 891 (s), 875 (w), 844 (s), 828 (s), 790 (vw), 762 (vw), 728 (w), 649 (w), 609 (s) cm^{-1}.

HRMS (EI): m/z for $C_{11}H_{11}F_3O_4S^+$ $[M]^+$: calcd.: 296.0325

found: 296.0317.

Tricyclo[4.4.0.0^{3,8}]dec-4-en-2-one (470)



489 **470**

To a mixture of enol triflate **489** (430 mg, 1.45 mmol, 1.00 eq.), *n*-Bu_3N (1.04 mL, 806 mg, 4.35 mmol, 3.00 eq.) and $Pd(PPh_3)Cl_2$ (102 mg, 0.145 mmol, 0.100 eq.) in degassed DMF (20.7 mL) was added formic acid (0.109 mL, 133 mg, 2.90 mmol, 2.00 eq.) and the resulting mixture was stirred at 60 °C for 1 h. The mixture was allowed to cool to room temperature and H_2O (15 mL) was added. The mixture was extracted with Et_2O (3 x 45 mL) and the combined organic layer was washed with 1 n HCl (2 x 60 mL), saturated aqueous $NaHCO_3$ (60 mL), brine (2 x 60 mL), dried (Na_2SO_4) and concentrated *in vacuo*. Purification of the residue by flash column chromatography (3 x 20 cm, silica, *n*-pentane : Et_2O = 4 : 1, 20 mL, #20–34) afforded alkene **470** (170 mg, 79%) as a colorless solid.

$C_{10}H_{12}O$ M_r = 148.20 g·mol^{-1}.

TLC R_f = 0.57 (hexanes : EtOAc = 3 : 1).

mp 150 – 153 °C.

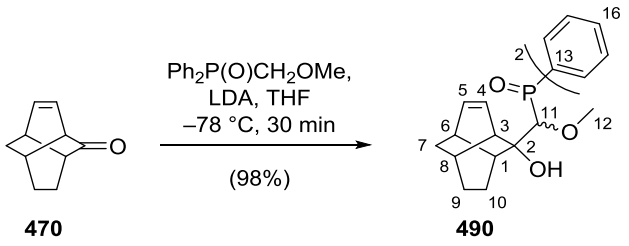
^{1}H NMR (600 MHz, $CDCl_3$): δ = 6.55 (ddd, $^3J_{C5\text{-}H,C4\text{-}H}$ = 7.3 Hz, $^3J_{C5\text{-}H,C6\text{-}H}$ = 6.0 Hz, $^4J_{C5\text{-}H,C3\text{-}H}$ = 0.8 Hz, 1H, C5-H), 5.92 (ddd, $^3J_{C4\text{-}H,C5\text{-}H}$ = 7.3 Hz, $^3J_{C4\text{-}H,C3\text{-}H}$ = 7.1 Hz, $^4J_{C4\text{-}H,C6\text{-}H}$ = 1.9 Hz, 1H, C4-H), 3.25 – 3.19 (m, 1H, C3-H), 2.94 – 2.87 (m, 1H, C6-H), 2.09 – 2.05 (m, 1H, C8-H), 2.05 – 2.02 (m, 1H, C1-H), 1.87 (ddd, $^2J_{C7\text{-}Hexo,C7\text{-}Hendo}$ = 11.6 Hz, $^3J_{C7\text{-}Hexo,C6\text{-}H}$ = 5.7 Hz, $^3J_{C7\text{-}Hexo,C8\text{-}H}$ = 1.2 Hz, 1H, C7-H_{exo}), 1.85 – 1.77 (m, 2H, C10-H), 1.72 – 1.67 (m, 1H, C9-H_A), 1.66 – 1.59 (m, 1H, C9-H_B), 1.22 (ddddd, $^2J_{C7\text{-}Hendo,C7\text{-}Hexo}$ = 11.6 Hz, $^3J_{C7\text{-}Hendo,C8\text{-}H}$ = 6.8 Hz, $^3J_{C7\text{-}Hendo,C6\text{-}H}$ = 2.0 Hz, $^4J_{C7\text{-}Hendo,C9\text{-}Hsyn}$ = 0.9 Hz, $^4J_{C7\text{-}Hendo,C1\text{-}H}$ = 0.9 Hz, 1H, C7-H_{endo}) ppm.

^{13}C NMR (150 MHz, $CDCl_3$): δ = 213.8 (C2), 140.9 (C5), 124.3 (C4), 54.9 (C3), 38.5 (C1), 36.3 (C6), 31.0 (C7), 27.6 (C8), 25.8 (C9), 25.1 (C10) ppm.

IR (ATR): $\tilde{\nu}$ = 3052 (vw), 2953 (w), 2929 (w), 2866 (vw), 1731 (vs), 1592 (vw), 1455 (vw), 1377 (vw), 1349 (vw), 1333 (vw), 1302 (vw), 1267 (vw), 1249 (vw), 1217 (vw), 1188 (vw), 1156 (vw), 1127 (vw), 1073 (vw), 1058 (vw), 1045 (vw), 1017 (vw), 972 (vw), 945 (vw), 903 (vw), 869 (vw), 846 (vw), 818 (vw), 791 (vw), 702 (w), 659 (vw) cm^{-1}.

HRMS (EI): m/z for $C_{10}H_{12}O^+$ $[M]^+$: calcd.: 148.0883
found: 148.0884.

((2-Hydroxytricyclo[4.4.0.0^{3,8}]dec-4-en-2-yl)(methoxy)methyl)diphenylphosphine oxide (490)



470 **490**

To a solution of diisopropylamine (10.8 mL, 7.71 g, 76.2 mmol, 4.95 eq.) in THF (100 mL) at 0 °C was added *n*-butyllithium (2.75 M in hexanes, 25.5 mL, 70.0 mmol, 4.55 eq.) and the resulting mixture was stirred at 0 °C for 30 min. To the mixture was added a solution of methoxymethyldiphenylphosphine oxide (20.7 g, 84.0 mmol, 5.45 eq.) in THF (150 mL) and the resulting solution was stirred at 0 °C for 15 min and was then cooled to –78 °C. At –78 °C a solution of ketone **470** (2.28 g, 15.4 mmol, 1.00 eq.) in THF (50.0 mL) was added dropwise and the resulting mixture was stirred at –78 °C for 30 min. The reaction was quenched by addition of saturated aqueous NH_4Cl, warmed to room temperature and the aqueous layer was extracted with Et_2O (3 x 200 mL). The combined organic layer was dried (Na_2SO_4) and concentrated *in vacuo*. Purification of the residue by flash column chromatography (5 x 20 cm, silica, hexanes : EtOAc = 1 : 1, 100 mL, #15–25) afforded the desired phosphine oxide **490** (5.40 g, 98%) as an inconsequential mixture of diastereomers in the form of a colorless solid. Recrystallization from EtOAc afforded crystals suitable for single crystal X-ray diffraction.

$C_{24}H_{27}O_3P$ M_r = 394.45 g·mol^{-1}.

TLC R_f = 0.26 (hexanes : EtOAc = 1 : 1).

mp 113 – 115 °C.

^{1}H NMR (600 MHz, $CDCl_3$, major isomer): δ = 7.94 – 7.84 (m, 4H, C14-H), 7.60 – 7.42 (m, 6H, C15-H, C16-H), 6.28 – 6.22 (ddd, $^3J_{C5\text{-}H,C4\text{-}H}$ = 7.5 Hz, $^3J_{C5\text{-}H,C6\text{-}H}$ = 6.2 Hz, $^4J_{C5\text{-}H,C3\text{-}H}$ = 1.5 Hz, 1H, C5-H), 5.31 (ddd, $^3J_{C4\text{-}H,C5\text{-}H}$ = 7.5 Hz, $^3J_{C4\text{-}H,C3\text{-}H}$ = 6.4 Hz, $^4J_{C4\text{-}H,C6\text{-}H}$ = 1.3 Hz, 1H, C4-H), 4.51 (d, $^2J_{C11\text{-}H,P}$ = 1.4 Hz, 1H, C11-H), 4.09 (s, 1H, OH), 2.94 (s, 3H, C12-H), 2.84 (dddd, $^3J_{C3\text{-}H,C4\text{-}H}$ = 6.4 Hz, $^3J_{C3\text{-}H,C8\text{-}H}$ = 6.3 Hz, $^4J_{C3\text{-}H,C1\text{-}H}$ = 1.7 Hz, $^4J_{C3\text{-}H,C5\text{-}H}$ = 1.5 Hz, 1H, C3-H), 2.55 – 2.49 (m, 1H, C6-H), 2.38 – 2.31 (m, 1H, C9-H_A), 1.86 (ddd, $^2J_{C10\text{-}Ha,C10\text{-}Hb}$ = 12.9 Hz, $^3J_{C10\text{-}Ha,C9\text{-}Ha}$ = 8.8 Hz, $^3J_{C10\text{-}Ha,C9\text{-}Hb}$ = 4.4 Hz, 1H, C10-H_A), 1.75 – 1.71 (m, 2H, C1-H, C7-H_A), 1.59 – 1.55 (m, 1H, C8-H), 1.53 – 1.47 (m, 1H, C10-H_B), 1.46 – 1.40 (m, 1H, C9-H_B), 0.99 – 0.94 (m, 1H, C7-H_B) ppm.

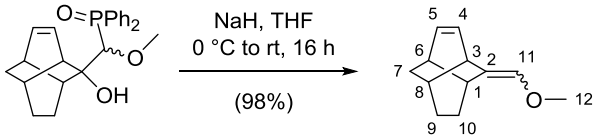
^{13}C NMR (75 MHz, $CDCl_3$, major isomer): δ = 136.5 (C5), 132.4 (d, $^2J_{C14,P}$ = 9.0 Hz, C14$_A$), 132.0 (C16$_A$), 131.9 (C16$_B$), 131.8 (d, $^2J_{C14,P}$ = 9.0 Hz, C14$_B$), 131.8 (C4), 131.4 (d, $^1J_{C13,P}$ = 99.6 Hz, C13), 128.8 (d, $^3J_{C15,P}$ = 11.4 Hz, C15$_A$), 128.2 (d, $^3J_{C15,P}$ = 11.4 Hz, C15$_B$), 85.4 (d, $^2J_{C2,P}$ = 1.9 Hz, C2), 85.3 (d, $^1J_{C11,P}$ = 81.2 Hz, C11), 61.5 (C12), 44.9

(C3), 38.0 (C7), 35.6 (C6), 29.3 (d, $^{3}J_{C1,P}$ = 7.5 Hz, C1), 26.7 (C9), 24.9 (C8), 21.0 (C10) ppm.

IR (ATR): $\tilde{\nu}$ = 3363 (vw), 2927 (w), 1436 (w), 1321 (vw), 1278 (vw), 1182 (w), 1158 (m), 1106 (m), 1085 (m), 1028 (w), 983 (w), 935 (vw), 816 (w), 799 (vw), 783 (vw), 751 (m), 744 (m), 723 (m), 696 (vs) cm^{-1}.

HRMS (EI): m/z for $C_{24}H_{27}O_3P^+$ $[M]^+$: calcd.: 394.1692
found: 394.1685.

2-(Methoxymethylene)tricyclo[4.4.0.0^{3,8}]dec-4-ene (491)



490 **491**

To a solution of phosphine oxide **490** (3.50 g, 8.87 mmol, 1.00 eq.) in THF (80.0 mL) at 0 °C was added NaH (2.13 g, 88.7 mmol, 10.0 eq.) portionwise. The resulting mixture was stirred at room temperature for 16 h and was then recooled to 0 °C and quenched by addition of H_2O (100 mL). The mixture was extracted with Et_2O (3 x 150 mL) and the combined organic layer was dried (Na_2SO_4) and concentrated *in vacuo*. Purification of the residue by flash column chromatography (4 x 24 cm, silica, *n*-pentane : Et_2O = 98 : 2, 20 mL, #13–23) afforded enol ether **491** (1.54 g, 98%) as an inconsequential mixture of isomers in the form of a colorless oil.

$C_{12}H_{16}O$ M_r = 176.26 g·mol^{-1}.

TLC R_f = 0.67 (*n*-pentane : Et_2O = 9 : 1).

^{1}H NMR (600 MHz, $CDCl_3$, major isomer): δ = 6.27 (ddd, $^{3}J_{C5\text{-}H,C4\text{-}H}$ = 7.7 Hz, $^{3}J_{C5\text{-}H,C6\text{-}H}$ = 6.2 Hz, $^{4}J_{C5\text{-}H,C3\text{-}H}$ = 1.1 Hz, 1H, C5-H), 6.10 (ddd, $^{3}J_{C4\text{-}H,C5\text{-}H}$ = 7.7 Hz, $^{3}J_{C4\text{-}H,C3\text{-}H}$ = 6.4 Hz, $^{3}J_{C4\text{-}H,C6\text{-}H}$ = 1.4 Hz, 1H, C4-H), 5.65 – 5.64 (m, 1H, C11-H), 3.47 (s, 3H, C12-H), 2.88 – 2.82 (m, 1H, C3-H), 2.71 – 2.66 (m, 1H, C6-H), 2.49 – 2.45 (m, 1H, C1-H), 1.77 (ddd, $^{2}J_{C7\text{-}H_A,C7\text{-}H_B}$ = 10.8 Hz, $^{3}J_{C7\text{-}H_A,C6\text{-}H}$ = 5.3 Hz, $^{3}J_{C7\text{-}H_A,C8\text{-}H}$ = 1.0 Hz, 1H, C7-H_A), 1.72 – 1.66 (m, 2H, C8-H, C10-H_A), 1.66 – 1.59 (m, 2H, C9-H_A, C10-H_B), 1.57 – 1.51 (m, 1H, C9-H_B), 1.07 – 1.02 (m, 1H, C7-H_B) ppm.

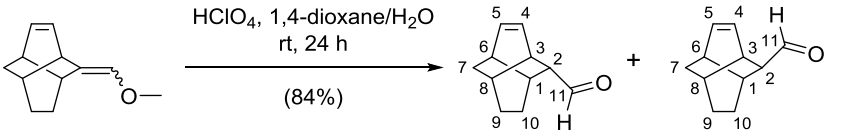
^{13}C NMR (150 MHz, $CDCl_3$, major isomer): δ = 136.5 (C5), 133.4 (C11), 131.7 (C4), 128.4 (C2), 59.4 (C12), 40.5 (C3), 35.5 (C6), 35.1 (C7), 28.2 (C1), 26.4 (C9), 24.9 (C8), 24.5 (C10) ppm.

IR (ATR): $\tilde{\nu}$ = 3044 (vw), 2931 (m), 2878 (vw), 2863 (w), 2830 (vw), 1723 (vw), 1698 (m), 1598 (vw), 1452 (w), 1361 (vw), 1350 (vw), 1329 (vw), 1313 (vw), 1300 (vw), 1272 (vw), 1238 (w), 1224 (m), 1218 (m), 1197 (w), 1178 (w), 1162 (vw), 1116 (vs),

1066 (w), 1026 (w), 1011 (vw), 980 (w), 938 (vw), 922 (vw), 872 (vw), 852 (vw), 834 (w), 820 (w), 798 (w), 787 (m), 772 (w), 758 (w), 682 (s), 662 (w) cm^{-1}.

HRMS (EI): m/z for $C_{12}H_{16}O^+$ $[M]^+$: calcd.: 176.1196
found: 176.1159.

Hydrolysis of Twistene Enol Ether 491



491 ***exo*-492** (9%) ***endo*-492** (75%)

To a solution of enolether **491** (1.53 g, 8.70 mmol, 1.00 eq.) in 9:1 1,4-dioxane:H_2O (256 mL) was added $HClO_4$ (35 wt-% in H_2O, 64.0 mL, 371 mmol, 42.6 eq.) and the resulting mixture was stirred at room temperature for 24 h. The mixture was poured to saturated aqueous $NaHCO_3$ (400 mL) and was extracted with Et_2O (3 x 250 mL). The combined organic layer was dried (Na_2SO_4) and concentrated *in vacuo*. Purification of the residue by flash column chromatography (4 x 20 cm, silica, *n*-pentane : Et_2O = 95 : 5, 20 mL) afforded *exo*-twistene aldehyde ***exo*-492** (#18–24, 126 mg 9%) as a colorless oil and *endo*-twistene aldehyde ***endo*-492** (#28–44, 1.06 g, 75%) as a colorless oil.

*Tricyclo[4.4.0.0^{3,8}]dec-4-ene-2-exo-carbaldehyde (**exo**-492)*

$C_{11}H_{14}O$ M_r = 162.23 g·mol^{-1}.

TLC R_f = 0.45 (hexanes : EtOAc = 9 : 1).

^{1}H NMR (600 MHz, $CDCl_3$): δ = 9.92 (s, 1H, C11-H), 6.34 (ddd, $^3J_{C4\text{-}H,C5\text{-}H}$ = 7.9 Hz, $^3J_{C4\text{-}H,C3\text{-}H}$ = 6.0 Hz, $^4J_{C4\text{-}H,C6\text{-}H}$ = 1.7 Hz, 1H, C4-H), 6.31 (ddd, $^3J_{C5\text{-}H,C4\text{-}H}$ = 7.9 Hz, $^3J_{C5\text{-}H,C6\text{-}H}$ = 6.0 Hz, $^4J_{C5\text{-}H,C3\text{-}H}$ = 1.7 Hz, 1H, C5-H), 3.11 (dddd, $^3J_{C3\text{-}H,C4\text{-}H}$ = 6.0 Hz, $^3J_{C3\text{-}H,C8\text{-}H}$ = 6.0 Hz, $^3J_{C3\text{-}H,C2\text{-}H}$ = 2.2 Hz, $^4J_{C3\text{-}H,C5\text{-}H}$ = 1.7 Hz, 1H, C3-H), 2.73 – 2.66 (m, 1H, C6-H), 2.12 – 2.06 (m, 1H, C1-H), 1.98 – 1.93 (dd, $^3J_{C2\text{-}H,C1\text{-}H}$ = 6.2 Hz, $^3J_{C2\text{-}H,C3\text{-}H}$ = 2.2 Hz, 1H, C2-H), 1.80 (dd, $^2J_{C7\text{-}Hexo,C7\text{-}Hendo}$ = 11.1, $^3J_{C7\text{-}Hexo,C6\text{-}H}$ = 5.5 Hz, 1H, C7-H_{exo}), 1.76 – 1.69 (m, 1H, C10-H_{anti}), 1.66 – 1.56 (m, 3H, C8-H, C9-H_{anti}, C10-H_{syn}), 1.36 – 1.29 (m, 1H, C9-H_{syn}), 1.07 – 1.01 (m, 1H, C7-H_{emdo}) ppm.

^{13}C NMR (150 MHz, $CDCl_3$): δ = 204.3 (C11), 136.0 (C5), 135.3 (C4), 61.6 (C2), 36.8 (C7), 35.1 (C6), 34.8 (C3), 25.0 (C1), 25.0 (C9), 23.1 (C8), 20.2 (C10) ppm.

IR (ATR): $\tilde{\nu}$ = 3418 (vw), 3044 (vw), 2937 (s), 2881 (m), 2806 (vw), 2702 (vw), 1806 (vw), 1714 (vs), 1598 (vw), 1484 (vw), 1461 (vw), 1391 (vw), 1352 (w), 1328 (vw), 1294 (vw), 1279 (vw), 1266 (vw), 1238 (vw), 1219 (vw), 1193 (vw), 1164 (vw), 1134 (vw), 1092 (w), 1050 (w), 1015 (w), 976 (w), 936 (vw), 902 (vw), 822 (vw), 787 (w), 740 (vw), 728 (vw), 689 (m) cm^{-1}.

HRMS (EI): m/z for $C_{11}H_{14}O^+$ $[M]^+$: calcd.: 162.1039
found: 162.1034.

*Tricyclo[4.4.0.0^{3,8}]dec-4-ene-2-endo-carbaldehyde (**endo**-**492**)*

$C_{11}H_{14}O$ M_r = 162.23 g·mol^{-1}.

TLC R_f = 0.38 (hexanes : EtOAc = 9 : 1).

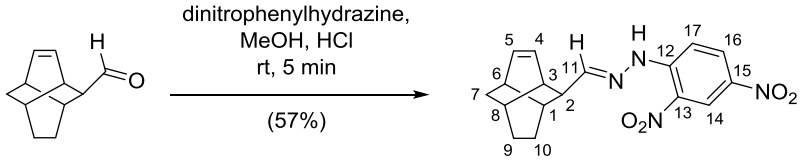
^{1}H NMR (400 MHz, $CDCl_3$): δ = 9.47 (s, 1H, C11-H), 6.55 (ddd, $^3J_{C5\text{-}H,C4\text{-}H}$ = 7.8 Hz, $^3J_{C5\text{-}H,C6\text{-}H}$ = 6.6 Hz, $^4J_{C5\text{-}H,C3\text{-}H}$ = 1.5 Hz, 1H, C5-H), 6.11 (ddd, $^3J_{C4\text{-}H,C5\text{-}H}$ = 7.8 Hz, $^3J_{C4\text{-}H,C3\text{-}H}$ = 6.1 Hz, $^4J_{C3\text{-}H,C6\text{-}H}$ = 1.5 Hz, 1H, C4-H), 3.20 – 3.16 (m, 1H, C3-H), 2.68 (dd, $^3J_{C2\text{-}H,C3\text{-}H}$ = 5.3 Hz, $^3J_{C2\text{-}H,C1\text{-}H}$ = 0.8 Hz, 1H, C2-H), 2.64 – 2.60 (m, 1H, C6-H), 2.35 – 2.31 (m, 1H, C1-H), 1.78 – 1.63 (m, 5H, C7-H_{exo}, C8-H, C9-H, C10-H_{anti}), 1.62 – 1.54 (m, 1H, C10-H_{syn}), 1.00 – 0.93 (m, 1H, C7-H_{endo}) ppm.

^{13}C NMR (100 MHz, $CDCl_3$): δ = 203.2 (C11), 142.1 (C5), 130.1 (C4), 58.5 (C2), 36.3 (C7), 36.0 (C3), 34.9 (C6), 28.7 (C1), 25.4 (C9), 24.4 (C10), 23.6 (C8) ppm.

IR (ATR): $\tilde{\nu}$ = 3045 (vw), 2938 (s), 2871 (m), 2809 (vw), 2708 (vw), 1769 (w), 1717 (vs), 1600 (vw), 1480 (vw), 1461 (vw), 1391 (vw), 1358 (w), 1312 (vw), 1300 (vw), 1271 (vw), 1237 (w), 1178 (w), 1136 (vw), 1112 (w), 1092 (w), 1075 (w), 1056 (w), 1039 (w), 1007 (w), 953 (w), 921 (w), 896 (w), 849 (vw), 814 (vw), 792 (m), 690 (m) cm^{-1}.

HRMS (EI): m/z for $C_{11}H_{14}O^+$ $[M]^+$: calcd.: 162.1039
found: 162.1045.

Tricyclo[4.4.0.0^{3,8}]dec-4-ene-2-*endo*-carbaldehyde 2,4-dinitrophenylhydrazone (493)



***endo*-492** **493**

Dinitrophenylhydrazine (58.5 mg, 0.294 mmol, 0.95 eq.) was dissolved in a mixture of MeOH (4.70 mL) and concentrated HCl (0.30 mL) by slight warming. To this mixture aldehyde ***endo*-492** (50.3 mg, 0.310 mmol, 1.00 eq.) was added and the mixture was stirred at room temperature for 5 min. The resulting orange precipitate was filtered off, washed with MeOH and dried *in vacuo* to afford the desired hydrazone **493** (60 mg, 57%) as an orange solid. Recrystallization from CH_2Cl_2/hexanes afforded crystals suitable for single crystal X-ray diffraction.

$C_{17}H_{18}N_4O_4$ M_r = 342.35 g·mol^{-1}.

TLC R_f = 0.71 (hexanes : EtOAc = 3 : 1).

mp 151 °C (dec.).

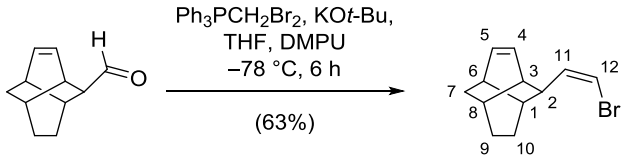
^{1}H NMR (400 MHz, DMSO-d_6): δ = 11.25 (s, 1H, N-H), 8.82 (d, $^{4}J_{C14\text{-}H,C16\text{-}H}$ = 2.7 Hz, 1H, C14-H), 8.30 (dd, $^{3}J_{C16\text{-}H,C17\text{-}H}$ = 9.7 Hz, $^{4}J_{C16\text{-}H,C14\text{-}H}$ = 2.7 Hz, 1H, C16-H), 7.79 (d, $^{3}J_{C17\text{-}H,C16\text{-}H}$ = 9.7 Hz, 1H, C17-H), 7.78 (d, $^{3}J_{C11\text{-}H,C2\text{-}H}$ = 3.8 Hz, 1H, C11-H), 6.53 (ddd, $^{3}J_{C5\text{-}H,C4\text{-}H}$ = 7.8 Hz, $^{3}J_{C5\text{-}H,C6\text{-}H}$ = 6.5 Hz, $^{4}J_{C5\text{-}H,C3\text{-}H}$ = 1.5 Hz, 1H, C5-H), 5.94 (ddd, $^{3}J_{C4\text{-}H,C5\text{-}H}$ = 7.8 Hz, $^{3}J_{C4\text{-}H,C3\text{-}H}$ = 5.9 Hz, $^{4}J_{C4\text{-}H,C6\text{-}H}$ = 1.2 Hz, 1H, C4-H), 3.02 – 2.93 (m, 2H, C2-H, C3-H), 2.67 – 2.60 (m, 1H, C6-H), 2.09 – 2.00 (m, 1H, C1-H), 1.87 – 1.68 (m, 3H, C7-H_A, C9-H_A, C10-H_A), 1.68 – 1.55 (m, 3H, C8-H, C9-H_B, C10-H_B), 0.97 – 0.89 (m, 1H, C7-H_B) ppm.

^{13}C NMR (100 MHz, DMSO-d_6): δ = 158.7 (C11), 144.7 (C12), 139.2 (C5), 136.2 (C15), 129.7 (C17), 129.1 (C4), 128.5 (C13), 123.1 (C14), 116.3 (C17), 47.2 (C2), 37.7 (C3), 36.1 (C7), 34.0 (C6), 28.7 (C1), 24.5 (C9*), 24.2 (C10*), 23.1 (C8) ppm.

IR (ATR): $\tilde{\nu}$ = 3298 (vw), 3047 (vw), 2944 (w), 2870 (vw), 1613 (s), 1585 (s), 1518 (m), 1495 (m), 1420 (m), 1358 (vw), 1321 (vs), 1301 (vs), 1264 (vs), 1220 (s), 1168 (w), 1128 (s), 1067 (s), 1055 (s), 970 (w), 943 (w), 920 (s), 872 (w), 859 (w), 829 (vs), 805 (w), 788 (m), 763 (w), 741 (vs), 717 (s), 690 (vs) cm^{-1}.

HRMS (EI): m/z for $C_{17}H_{18}N_4O_4^+$ $[M]^+$: calcd.: 342.1323
found: 342.1317.

2((*Z*)-2-Bromoalkenyl)tricyclo[4.4.0.0^{3,8}]dec-4-ene (463)



***endo*-492** **463**

To a solution of (bromomethyl)triphenylphosphonium bromide (297 mg, 0.682 mmol, 1.10 eq.) in THF (4.00 mL) at –78 °C was added KO*t*-Bu (76.5 mg, 0.682 mmol, 1.10 eq.). The resulting yellow reaction mixture was stirred at –78 °C for 15 min, after which time DMPU (0.351 mL, 373 mg, 2.91 mmol, 4.70 eq.) and aldehyde ***endo*-492** (101 mg, 0.620 mmol, 1.00 eq.) in THF (1.00 mL) were added successively. The mixture was stirred for an additional 6 h at –78 °C and was then diluted with *n*-pentane (10 mL) and filtered over celite. The residue was washed with *n*-pentane (20 mL) and the combined filtrates were concentrated *in vacuo*. Purification of the residue by flash column chromatography (2 x 15 cm, silica, *n*-pentane, 8 mL, #8─10) afforded alkenyl bromide **463** (94 mg, 63%) as a colorless oil.

$C_{12}H_{15}Br$ M_r = 239.16 g·mol^{-1}.

TLC R_f = 0.93 (hexanes : EtOAc = 1 : 1).

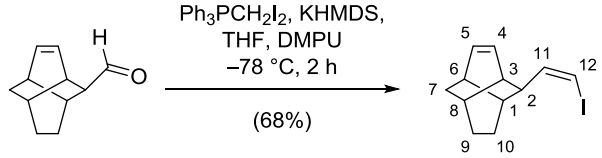
^{1}H NMR (600 MHz, $CDCl_3$): δ = 6.48 (ddd, $^3J_{C5\text{-}H,C6\text{-}H}$ = 7.9 Hz, $^3J_{C5\text{-}H,C4\text{-}H}$ = 6.2 Hz, $^4J_{C5\text{-}H,C3\text{-}H}$ = 1.5 Hz, 1H, C5-H), 6.00 (dd, $^3J_{C11\text{-}H,C12\text{-}H}$ = 7.4 Hz, $^3J_{C11\text{-}H,C2\text{-}H}$ = 6.9 Hz, 1H, C11-H), 5.97 – 5.94 (m, 2H, C4-H, C12-H), 3.12 – 3.07 (m, 1H, C2-H), 2.88 – 2.84 (m, 1H, C3-H), 2.61 – 2.57 (m, 1H, C6-H), 1.92 – 1.83 (m, 1H, C9-H_A), 1.77 – 1.66 (m, 3H, C7-H_A, C10-H), 1.63 – 1.57 (m, 2H, C8-H, C9-H_B), 1.49 – 1.46 (m, 1H, C1-H), 1.05 – 0.98 (m, 1H, C7-H_B) ppm.

^{13}C NMR (150 MHz, $CDCl_3$): δ = 140.2 (C11), 137.8 (C5), 130.5 (C4), 105.0 (C12), 45.2 (C2), 37.9 (C3), 37.0 (C7), 34.6 (C6), 31.5 (C1), 25.2 (C10), 25.0 (C9), 23.8 (C8) ppm.

IR (ATR): $\tilde{\nu}$ = 3043 (vw), 2937 (vs), 2876 (m), 1611 (vw), 1480 (vw), 1460 (vw), 1450 (vw), 1354 (vw), 1331 (vw), 1320 (vw), 1298 (m), 1286 (w), 1246 (vw), 1210 (vw), 1181 (vw), 1166 (vw), 1136 (vw), 1116 (vw), 1070 (vw), 1054 (vw), 1037 (vw), 965 (vw), 944 (vw), 908 (vw), 878 (vw), 858 (vw), 848 (vw), 806 (w), 792 (s), 744 (w), 704 (m), 682 (vs) cm^{-1}.

HRMS (EI): m/z for $C_{12}H_{15}Br^+$ $[M]^+$: calcd.: 238.0352
found: 238.0346.

2((*Z*)-2-Iodoalkenyl)tricyclo[4.4.0.0^{3,8}]dec-4-ene (464)



***endo*-492** **464**

To a suspension of (iodomethyl)triphenylphosphonium iodide (723 mg, 1.36 mmol, 2.20 eq.) in THF (7.00 mL) at 0 °C was slowly added a solution of NaHMDS (1.00 M in THF, 1.36 mL, 1.36 mmol, 2.20 eq.). The resulting yellow reaction mixture was stirred at 0 °C for 5 min, after which time the reaction mixture was cooled to –78 °C and DMPU (0.702 mL, 747 mg, 5.83 mmol, 9.40 eq.) and a solution of aldehyde ***endo*-492** (101 mg, 0.620 mmol, 1.00 eq.) in THF (3.00 mL) were added. The mixture was stirred at –78 °C for 2 h and was then diluted with *n*-pentane (20 mL). The resulting slurry was filtered over celite and the residue was washed with *n*-pentane (50 mL). The combined filtrate was concentrated *in vacuo*. Purification of the residue by flash column chromatography (2 x 16 cm, silica, hexanes, 8 mL, #6–8) yielded alkenyl iodide **464** (120 mg, 68%) as a brown oil.

$C_{12}H_{15}I$ M_r = 286.16 g·mol^{-1}.

TLC R_f = 0.77 (hexanes).

^{1}H NMR (400 MHz, $CDCl_3$): δ = 6.48 (ddd, $^3J_{C5\text{-}H,C6\text{-}H}$ = 7.6 Hz, $^3J_{C5\text{-}H,C4\text{-}H}$ = 6.1 Hz, $^4J_{C5\text{-}H,C3\text{-}H}$ = 1.3 Hz, 1H, C5-H), 6.09 (dd, $^3J_{C11\text{-}H,C12\text{-}H}$ = 7.2 Hz, $^3J_{C11\text{-}H,C2\text{-}H}$ = 7.2 Hz, 1H, C11-H), 5.98 (dd, $^3J_{C12\text{-}H,C11\text{-}H}$ = 7.2 Hz, $^4J_{C12\text{-}H,C2\text{-}H}$ = 1.1 Hz, 1H, C12-H), 5.94

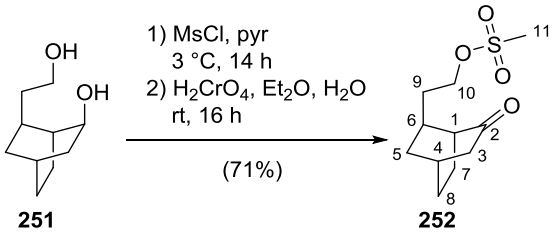
(ddd, $^{3}J_{C4\text{-}H,C3\text{-}H}$ = 7.8 Hz, $^{3}J_{C4\text{-}H,C5\text{-}H}$ = 6.1 Hz, $^{4}J_{C4\text{-}H,C6\text{-}H}$ = 1.4 Hz, 1H, C4-H), 2.94 – 2.90 (m, 1H, C2-H), 2.90 – 2.86 (m, 1H, C3-H), 2.63 – 2.58 (m, 1H, C6-H), 1.92 – 1.84 (m, 1H, C9-H_A), 1.79 – 1.67 (m, 3H, C7-H_A, C10-H), 1.63 – 1.57 (m, 2H, C8-H, C9-H_B), 1.51 – 1.47 (m, 1H, C1-H), 1.04 – 0.98 (m, 1H, C7-H_B) ppm.

^{13}C NMR (100 MHz, $CDCl_3$): δ = 146.5 (C11), 137.9 (C5), 130.6 (C4), 79.3 (C12), 49.8 (C2), 37.8 (C3), 37.1 (C7), 34.7 (C6), 31.3 (C1), 25.3 (C10), 25.0 (C9), 23.7 (C8) ppm.

IR (ATR): $\tilde{\nu}$ = 3042 (vw), 2938 (vs), 2875 (w), 1681 (vw), 1599 (vw), 1480 (vw), 1459 (vw), 1450 (vw), 1354 (vw), 1277 (m), 1268 (w), 1210 (vw), 1181 (vw), 1162 (vw), 1136 (vw), 1114 (vw), 1075 (vw), 1004 (vw), 907 (vw), 877 (vw), 848 (vw), 806 (w), 792 (m), 738 (vw), 700 (w), 679 (s) cm^{-1}.

HRMS (EI): m/z for $C_{12}H_{15}I^{+}$ $[M]^{+}$: calcd.: 286.0213
found: 286.0196.

6-*endo*-(2-Mesyloxyethyl)-bicyclo[2.2.2]octan-2-one (252)



251 **252**

To a solution of diol **251** (645 mg, 3.79 mmol, 1.00 eq.) in pyridine (2.50 mL) at 0 °C was added dropwise MsCl (0.324 mL, 479 mg, 4.19 mmol, 1.10 eq.). The mixture was allowed to stand at 3 °C for 14 h, then 1.0 mL H_2O were added and the resulting solution was stirred at 0 °C for 30 min. The reaction mixture was poured into a mixture of ice and 1 M HCl (5 mL) and the aqueous layer was extracted with Et_2O (5 x 10 mL). The combined organic layer was washed with water (15 mL), brine (15 mL), dried (Na_2SO_4) and concentrated *in vacuo* to about 10 mL. To this solution containing the crude mesylate was added a mixture of sodium dichromate dihydrate (473 mg, 1.59 mmol, 0.419 eq.) in H_2O (2.4 mL) and H_2SO_4 (0.36 mL, 6.67 mmol, 1.76 eq.). The resulting mixture was stirred at room temperature for 16 h and was then poured into water (30 mL) and extracted with Et_2O (3 x 30 mL). The combined organic layer was washed with water (2 x 50 mL), brine (2 x 50 mL), dried (Na_2SO_4) and concentrated *in vacuo*. Purification of the residue by flash column chromatography (4 x 21 cm, silica, hexanes : EtOAc = 1 : 1, 20 mL, #35–71) afforded ketomesylate **252** (660 mg, 71%) as a colorless oil.

$C_{11}H_{18}O_4S$ M_r = 246.33 g·mol^{-1}.

TLC R_f = 0.34 (hexanes : EtOAc = 1 : 1).

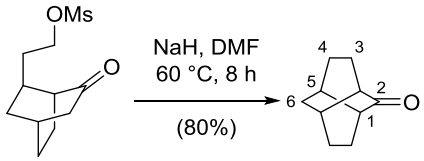
^{1}H NMR (600 MHz, $CDCl_3$): δ = 4.27 – 4.19 (m, 2H, C10-H), 2.99 (s, 3H, C11-H), 2.24 (ddd, $^{2}J_{C3\text{-}Hendo,C3\text{-}Hexo}$ = 18.8 Hz, $^{3}J_{C3\text{-}Hendo,C4\text{-}H}$ = 2.7 Hz, $^{4}J_{C3\text{-}Hendo,C8\text{-}Hanti}$ = 2.7 Hz, 1H, C3-H_{endo}*), 2.21 – 2.18 (m, 1H, C4-H), 2.17 (dd, $^{3}J_{C1\text{-}H,C7\text{-}Hsyn}$ = 5.4 Hz, $^{3}J_{C1\text{-}H,C6\text{-}H}$ = 2.8 Hz, 1H, C1-H), 2.16 – 2.10 (m, 2H, C3-H_{exo}*, C6-H), 2.03 (dddd, $^{2}J_{C5\text{-}Hexo,C5\text{-}Hendo}$ = 13.3 Hz, $^{3}J_{C5\text{-}Hexo,C6\text{-}H}$ = 10.4 Hz, $^{3}J_{C5\text{-}Hexo,C4\text{-}H}$ = 3.5 Hz, $^{4}J_{C5\text{-}Hexo,C3\text{-}Hexo}$ = 2.7 Hz, 1H, C5-H_{exo}), 1.87 – 1.79 (m, 2H, C7-H), 1.72 – 1.61 (m, 3H, C8-H, C9-H_A), 1.61 – 1.53 (m, 1H, C9-H_B), 1.13 (dddd, $^{2}J_{C5\text{-}Hendo,C5\text{-}Hexo}$ = 13.3 Hz, $^{2}J_{C5\text{-}Hendo,C4\text{-}H}$ = 5.5 Hz, $^{3}J_{C5\text{-}Hendo,C6\text{-}H}$ = 2.7 Hz, $^{4}J_{C5\text{-}Hendo,C8\text{-}Hsyn}$ = 2.7 Hz, 1H, C5-H_{endo}) ppm.

^{13}C NMR (150 MHz, $CDCl_3$): δ = 216.4 (C2), 67.4 (C10), 47.2 (C1), 44.9 (C3), 37.5 (C11), 36.3 (C9), 33.0 (C5), 32.5 (C6), 28.0 (C4), 23.6 (C8), 23.1 (C7) ppm.

IR (ATR): $\tilde{\nu}$ = 3023 (vw), 2936 (w), 2869 (vw), 1717 (s), 1471 (vw), 1455 (vw), 1403 (vw), 1348 (s), 1226 (vw), 1201 (vw), 1169 (vs), 1134 (vw), 1103 (w), 1069 (vw), 1033 (vw), 965 (m), 951 (m), 935 (s), 896 (m), 860 (w), 828 (w), 816 (w), 800 (w), 727 (vw) cm^{-1}.

HRMS (EI): m/z for $C_{11}H_{18}O_4S^+$ $[M]^+$: calcd.: 246.0920
found: 246.0923.

Tricyclo[4.4.0.0^{3,8}]decan-2-one (253)



252 **253**

A solution of ketomesylate **252** (1.91 g, 7.75 mmol, 1.00 eq.) and sodium hydride (651 mg, 27.1 mmol, 3.50 eq.) in DMF (51.7 mL) was heated to 60 °C for 8 h after which time the reaction mixture was cooled to 0 °C. Excess sodium hydride was destroyed by addition of methanol and the reaction mixture was poured on H_2O (50 mL). The aqueous layer was extracted with *n*-pentane (5 x 50 mL) and the combined organic layer was washed with 1 M HCl (100 mL), brine (100 mL), dried (Na_2SO_4) and concentrated *in vacuo*. Purification of the residue by flash column chromatography (5 x 10 cm, silica, hexanes : EtOAc = 9 : 1, 20 mL, #27–47) afforded twistanone **253** (929 mg, 80%) as a colorless solid.

$C_{10}H_{14}O$ M_r = 150.22 g·mol^{-1}.

TLC R_f = 0.19 (hexanes : EtOAc = 1 : 1).

mp 197 – 199 °C.

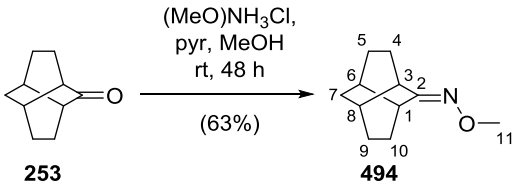
^{1}H NMR (400 MHz, $CDCl_3$): δ = 2.28 – 2.20 (m, 4H, C1-H, C5-H), 1.96 – 1.85 (m, 2H, C3-H_{endo}*), 1.82 – 1.73 (m, 2H, C3-H_{exo}*), 1.62 – 1.55 (m, 4H, C4-H_{endo}**, C6-H), 1.51 – 1.40 (m, 2H, C4-H_{exo}) ppm.

^{13}C NMR (75 MHz, $CDCl_3$): δ = 224.8 (C2), 48.6 (C1), 32.9 (C5), 25.9 (C4), 25.5 (C6), 24.7 (C3) ppm.

IR (ATR): $\tilde{\nu}$ = 2937 (m), 2864 (m), 1730 (vs), 1466 (vw), 1447 (vw), 1327 (vw), 1306 (vw), 1273 (vw), 1248 (vw), 1229 (vw), 1213 (vw), 1134 (vw), 1146 (vw), 1078 (w), 1064 (vw), 1043 (vw), 1023 (vw), 1013 (vw), 916 (w), 871 (vw), 811 (vw), 793 (vw), 730 (m) cm^{-1}.

HRMS (EI): m/z for $C_{10}H_{14}O^+$ $[M]^+$: calcd.: 150.1039
found: 150.1034.

O-Methyltricyclo[4.4.0.0^{3,8}]decan-2-one oxime (494)



To a solution of ketone **253** (225 mg, 1.50 mmol, 1.00 eq.) in MeOH (3.43 mL) was added pyridine (267 µL, 261 mg, 3.30 mmo, 2.20 eq.) and methoxylamine hydrochloride (200 mg, 2.40 mmol, 1.60 eq.) and the resulting mixture was stirred at room temperature for 48 h. The reaction mixture was concentrated *in vacuo* and the residue was diluted with H_2O (20 mL) and extracted with CH_2Cl_2 (5 x 20 mL). The combined organic layer was washed with 10 wt-% aqueous $CuSO_4$ (3 x 20 mL), dried (Na_2SO_4) and concentrated *in vacuo*. Purification of the residue by flash column chromatography (3 x 25 cm, silica, hexanes : EtOAc = 9 : 1, 20 mL, #12–19) afforded oxime ether **494** (170 mg, 63%) as a colorless solid.

$C_{11}H_{17}ON$ M_r = 179.26 g·mol^{-1}.

TLC R_f = 0.46 (hexanes : EtOAc = 9 : 1).

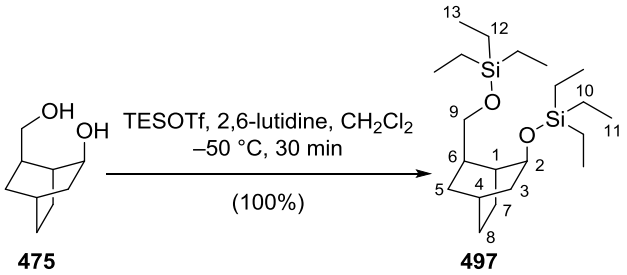
^{1}H NMR (600 MHz, $CDCl_3$): δ = 3.80 (s, 3H, C11-H), 3.06 – 2.99 (m, 1H, C3-H), 2.33 – 2.30 (m, 1H, C1-H), 2.05 – 2.01 (m, 1H, C6-H), 1.99 – 1.94 (m, 1H, C8-H), 1.78 (dddd, $^{2}J_{C10\text{-}H_A,C10\text{-}H_B}$ = 12.5 Hz, $^{2}J_{C10\text{-}H_A,C9\text{-}H_A}$ = 9.8 Hz, $^{2}J_{C10\text{-}H_A,C1\text{-}H}$ = 9.0 Hz, $^{2}J_{C10\text{-}H_A,C9\text{-}H_B}$ = 1.4 Hz, 1H, C10-H_A), 1.71 – 1.64 (m, 3H, C4-H, C10-H_B), 1.55 – 1.38 (m, 6H, C5-H, C7-H, C9-H) ppm.

^{13}C NMR (150 MHz, $CDCl_3$): δ = 168.4 (C2), 61.0 (C11), 37.8 (C1), 34.2 (C3), 30.2 (C6), 30.1 (C8), 26.2 (C5*), 25.8 (C7*), 25.5 (C9*), 24.9 (C10), 22.6 (C4) ppm.

IR (ATR): $\tilde{\nu}$ = 2930 (s), 2862 (m), 2811 (vw), 1658 (vw), 1479 (vw), 1463 (w), 1445 (w), 1383 (vw), 1361 (vw), 1328 (vw), 1303 (vw), 1278 (vw), 1228 (vw), 1194 (vw), 1163 (vw), 1138 (vw), 1110 (w), 1102 (w), 1049 (vs), 1042 (vs), 1005 (vw), 980 (vw), 960 (vw), 923 (vw), 903 (w), 884 (s), 856 (s), 833 (s), 804 (vw), 793 (w), 765 (w), 671 (vw) cm^{-1}.

HRMS (EI): m/z for $C_{11}H_{17}ON^+$ $[M]^+$: calcd.: 179.1305
found: 179.1298.

2-*endo*-Triethylsiloxy-6-*endo*-triethylsiloxymethylbicyclo[2.2.2]octane (497)



475 **497**

To a solution of diol **475** (1.00 g, 6.40 mmol, 1.00 eq.) in CH_2Cl_2 (110 mL) at ─50 °C was added 2,6-lutidine (2.24 mL, 2.06 g, 19.2 mmol, 3.00 eq.). The reaction mixture was treated dropwise with TESOTf (3.65 mL, 4.23 g, 16.0 mmol, 2.5 eq.) and stirred for 30 min at ─50 °C. The reaction was quenched by addition of saturated aqueous $NaHCO_3$ (100 mL) and the organic layer was extracted with CH_2Cl_2 (3 x 100 mL). The combined organic layer was dried (Na_2SO_4) and concentrated *in vacuo*. Purification of the residue by flash column chromatography (5 x 25 cm, silica, hexanes : Et_2O = 95 : 5, 100 mL, #6─10) afforded protected diol **497** (2.46 g, 100%) as a colorless oil.

$C_{21}H_{44}O_2Si_2$ M_r = 384.75 g·mol^{-1}.

TLC R_f = 0.86 (hexanes : EtOAc = 9 : 1).

^{1}H NMR (600 MHz, $CDCl_3$): δ = 3.85 (dddd, $^3J_{C2\text{-}H,C3\text{-}Hexo}$ = 9.5 Hz, $^3J_{C2\text{-}H,C3\text{-}Hendo}$ = 3.4 Hz, $^3J_{C2\text{-}H,C1\text{-}H}$ = 3.4 Hz, $^4J_{C2\text{-}H,C6\text{-}H}$ = 1.6 Hz, 1H, C2-H), 3.83 (dd, $^2J_{C9\text{-}H_A,C9\text{-}H_B}$ = 9.8 Hz, $^3J_{C9\text{-}H_A,C6\text{-}H}$ = 9.0 Hz, 1H, C9-H_A), 3.68 (dd, $^2J_{C9\text{-}H_B,C9\text{-}H_A}$ = 9.8 Hz, $^3J_{C9\text{-}H_B,C6\text{-}H}$ = 4.5 Hz, 1H, C9-H_B), 1.89 (dddd, $^2J_{C3\text{-}Hexo,C3\text{-}Hendo}$ = 13.5 Hz, $^3J_{C3\text{-}Hexo,C2\text{-}H}$ = 9.5 Hz, $^3J_{C3\text{-}Hexo,C4\text{-}H}$ = 3.0 Hz, $^4J_{C3\text{-}Hexo,C5\text{-}Hexo}$ = 3.0 Hz, 1H, C3-H_{exo}), 1.83 (dddddd, $^3J_{C6\text{-}H,C5\text{-}Hexo}$ = 10.5 Hz, $^3J_{C6\text{-}H,C9\text{-}H_A}$ = 9.0 Hz, $^3J_{C6\text{-}H,C5\text{-}Hendo}$ = 5.9 Hz, $^3J_{C6\text{-}H,C9\text{-}H_B}$ = 4.5 Hz, $^3J_{C6\text{-}H,C1\text{-}H}$ = 1.6 Hz, $^4J_{C6\text{-}H,C2\text{-}H}$ = 1.6 Hz, 1H, C6-H), 1.78 (dddd, $^2J_{C5\text{-}Hexo,C5\text{-}Hendo}$ = 13.1 Hz, $^3J_{C5\text{-}Hexo,C6\text{-}H}$ = 10.5 Hz, $^3J_{C5\text{-}Hexo,C4\text{-}H}$ = 3.8 Hz, $^4J_{C5\text{-}Hexo,C3\text{-}Hexo}$ = 3.0 Hz, 1H, C5-H_{exo}), 1.68 – 1.65 (m, 1H, C4-H), 1.58 (m, 1H, C1-H), 1.53 – 1.48 (m, 1H, C7-H_A), 1.46 – 1.41 (m, 1H, C8-H_A), 1.41 – 1.28 (m, 4H, C3-H_{endo}, C5-H_{endo}, C7-H_B, C8-H_B), 0.96 (t, $^3J_{C11\text{-}H,C10\text{-}H}$ = 7.9 Hz, 9H, C11-H*), 0.95

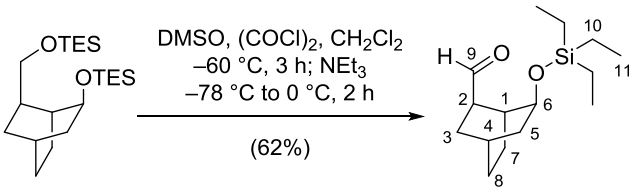
(t, $^3J_{C13\text{-}H,C12\text{-}H}$ = 7.9 Hz, 9H, C13-H*), 0.59 (q, $^3J_{C10\text{-}H,C11\text{-}H}$ = 7.9 Hz, 6H, C10-H**), 0.55 (q, $^3J_{C12\text{-}H,C13\text{-}H}$ = 7.9 Hz, 6H, C12-H**) ppm.

^{13}C NMR (150 MHz, $CDCl_3$): δ = 70.7 (C2), 69.5 (C9), 39.5 (C3), 39.2 (C6), 34.4 (C1), 32.2 (C5), 25.6 (C7), 25.2 (C4), 23.8 (C8), 7.0 (C11), 7.0 (C13), 5.0 (C10*), 4.7 (C12*) ppm.

IR (ATR): $\tilde{\nu}$ = 2953 (m), 2937 (m), 2911 (m), 2876 (m), 2733 (vw), 1458 (w), 1414 (w), 1383 (vw), 1331 (vw), 1238 (w), 1169 (vw), 1146 (vw), 1102 (s), 1074 (s), 1056 (vs), 1005 (s), 972 (w), 886 (vw), 858 (w), 837 (vw), 805 (m), 768 (w), 738 (vs), 726 (vs), 685 (w) cm^{-1}.

HRMS (EI): m/z for $C_{19}H_{39}O_2Si_2^+$ $[M-Et]^+$: calcd.: 355.2483
found: 355.2484.

6-*endo*-Triethylsiloxybicyclo[2.2.2]octane-2-*endo*-carbaldehyde (498)



497 **498**

A solution of DMSO (100 µL, 0.110 g, 1.40 mmol, 2.70 eq.) in CH_2Cl_2 (2.00 mL) was added dropwise to a solution of oxalyl chloride (2.00 m in CH_2Cl_2, 0.338 mL, 0.676 mmol, 1.30 eq.) in CH_2Cl_2 (6.00 mL) at –78 °C. The internal temperature was monitored during the addition to insure that the temperature did not rise above –50 °C. At –78 °C a solution of diol **497** (0.200 g, 0.520 mmol, 1.00 eq.) in CH_2Cl_2 (4.00 mL) was added dropwise to the dimethylchlorosulfonium chloride solution and the resulting mixture was stirred for 3 h at –60 °C. The reaction mixture was recooled to –78 °C and triethylamine (0.361 mL, 0.263 g, 2.60 mmol, 5.00 eq.) was added in one portion. The reaction mixture was stirred for an additional 10 min at –78 °C. The solution was slowly warmed to 0 °C over the course of 30 min and maintained at 0 °C for 1 h. The cold solution was partitioned between saturated aqueous $NaHCO_3$ (15 mL) and CH_2Cl_2 (10 mL). The layers were separated and the aqueous layer was extracted with CH_2Cl_2 (3 × 15 mL). The combined organic layers were washed with brine (25 mL), dried (Na_2SO_4) and concentrated *in vacuo*. Purification of the residue by flash column chromatography (2 x 25 cm, silica, *n*-pentane : Et_2O = 9 : 1, 8 mL, #19–24) afforded aldehyde **498** (87 mg, 62%) as a colorless oil.

$C_{15}H_{28}O_2Si$ M_r = 268.47 g·mol^{-1}.

TLC R_f = 0.58 (hexanes : EtOAc = 9 : 1).

^{1}H NMR (300 MHz, $CDCl_3$): δ = 9.66 (d, $^3J_{C9\text{-}H,C2\text{-}H}$ = 0.4 Hz, 1H, C9-H), 3.88 (ddd, $^3J_{C6\text{-}H,C5\text{-}Hexo}$ = 9.0 Hz, $^3J_{C6\text{-}H,C5\text{-}Hendo}$ = 4.0 Hz, $^3J_{C6\text{-}H,C1\text{-}H}$ = 2.2 Hz, 1H, C6-H), 2.28 –

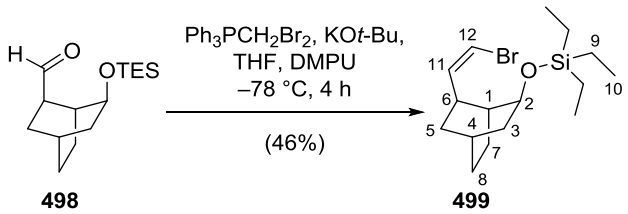
2.17 (m, 2H, C1-H, C2-H), 2.10 (dddd, $^{2}J_{\text{C3-Hendo,C3-Hexo}}$ = 13.0 Hz, $^{3}J_{\text{C3-Hendo,C2-H}}$ = 6.2 Hz, $^{3}J_{\text{C3-Hendo,C4-H}}$ = 2.2 Hz, $^{4}J_{\text{C3-Hendo,C8-Hanti}}$ = 2.2 Hz, 1H, C3-H_{endo}), 1.83 (dddd, $^{2}J_{\text{C5-Hexo,C5-Hendo}}$ = 13.7 Hz, $^{3}J_{\text{C5-Hexo,C6-H}}$ = 9.0 Hz, $^{3}J_{\text{C5-Hexo,C4-H}}$ = 2.8 Hz, $^{4}J_{\text{C5-Hexo,C3-Hexo}}$ = 2.8 Hz, 1H, C5-H_{exo}), 1.74 (m, 1H, C4-H), 1.70 – 1.56 (m, 2H, C3-H_{exo}, C7-H_A), 1.55 – 1.29 (m, 4H, C5-H_{endo}, C7-H_B, C8-H), 0.95 – 0.89 (m, 9H, C11-H), 0.58 – 0.49 (m, 6H, C10-H) ppm.

^{13}C NMR (75 MHz, $CDCl_3$): δ = 204.7 (C9), 69.2 (C6), 46.7 (C2), 38.5 (C5), 35.9 (C1), 26.0 (C3), 24.4 (C8), 24.0 (C4), 23.1 (C7), 6.9 (C11), 4.9 (C10) ppm.

IR (ATR): $\tilde{\nu}$ = 3420 (vw), 2937 (m), 2912 (m), 2874 (m), 2812 (vw), 2707 (vw), 1783 (vw), 1724 (s), 1456 (w), 1414 (vw), 1374 (vw), 1359 (vw), 1332 (vw), 1304 (vw), 1278 (vw), 1239 (w), 1184 (vw), 1169 (w), 1136 (vw), 1104 (m), 1050 (vs), 1006 (s), 977 (m), 967 (m), 931 (w), 897 (vw), 856 (m), 810 (m), 770 (m), 724 (vs), 686 (w) cm^{-1}.

HRMS (EI): m/z for $C_{15}H_{28}O_2Si^+$ $[M]^+$: calcd.: 268.1853
found: 268.1864.

6-*endo*-(*Z*)-2-Bromoalkenyl-2-*endo*-triethylsiloxybicyclo[2.2.2]octane (499)



498 **499**

To a solution of (bromomethyl)triphenylphosphonium bromide (154 mg, 0.353 mmol, 1.10 eq.) in THF (3.00 mL) was added KO*t*-Bu (39.6 mg, 0.353 mmol, 1.10 eq.) at –78 °C. The resulting yellow reaction mixture was stirred at –78 °C for 15 min, after which time DMPU (0.182 mL, 193 mg, 1.51 mmol, 4.70 eq.) and a solution of aldehyde **498** (86.2 mg, 0.321 mmol, 1.00 eq.) in THF (1.00 mL) were added successively. The mixture was stirred for an additional 4 h at –78 °C and was then diluted with hexanes (10 mL) and filtered over celite. The residue was washed with hexanes and the combined filtrate was concentrated *in vacuo*. Purification of the residue by flash column chromatography (2 x 29 cm, silica, *n*-pentane : Et_2O = 95 : 5, 8 mL, #8–11) afforded alkenylbromide **499** (28 mg, 25%) as a colorless oil.

$C_{16}H_{29}OSi$ M_r = 345.40 g·mol^{-1}.

TLC R_f = 0.92 (hexanes).

^{1}H NMR (400 MHz, $CDCl_3$): δ = 6.61 (dd, $^{3}J_{\text{C11-H,C6-H}}$ = 8.7 Hz, $^{3}J_{\text{C11-H,C12-H}}$ = 6.7 Hz, 1H, C11-H), 5.93 (dd, $^{3}J_{\text{C12-H,C11-H}}$ = 6.7 Hz, $^{4}J_{\text{C12-H,C6-H}}$ = 1.1 Hz, 1H, C12-H), 3.91 (dddd, $^{3}J_{\text{C2-H,C3-Hexo}}$ = 9.2 Hz, $^{3}J_{\text{C2-H,C3-Hendo}}$ = 3.8 Hz, $^{3}J_{\text{C2-H,C1-H}}$ = 2.5 Hz, $^{4}J_{\text{C2-H,C6-H}}$ = 1.2 Hz,

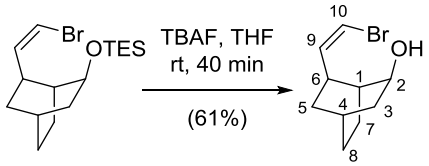
1H, C2-H), 2.84 – 2.75 (m, 1H, C6-H), 1.94 – 1.83 (m, 2H, C3-H_A, C5-H_A), 1.73 – 1.68 (m, 2H, C1-H, C4-H), 1.67 – 1.60 (m, 1H, C7-H_A), 1.51 – 1.30 (m, 5H, C3-H_B, C5-H_B, C7-H_B, C8-H), 0.94 (t, $^3J_{C10\text{-}H,C9\text{-}H}$ = 7.9 Hz, 9H, C10-H), 0.55 (q, $^3J_{C9\text{-}H,C10\text{-}H}$ = 7.9 Hz, 6H, C9-H) ppm.

^{13}C NMR (100 MHz, $CDCl_3$): δ = 143.0 (C11), 103.9 (C12), 70.4 (C2), 39.2 (C3), 36.3 (C1), 35.9 (C6), 32.6 (C5), 24.7 (C4), 24.6 (C7), 23.4 (C8), 7.1 (C10), 5.0 (C9) ppm.

IR (ATR): $\tilde{\nu}$ = 3080 (vw), 2935 (s), 2874 (m), 1615 (vw), 1454 (w), 1438 (vw), 1414 (w), 1380 (w), 1359 (vw), 1331 (vw), 1281 (w), 1239 (w), 1168 (w), 1137 (vw), 1103 (vs), 1090 (m), 1078 (w), 1060 (vs), 1006 (s), 976 (m), 930 (w), 865 (m), 838 (w), 811 (m), 796 (vw), 768 (m), 740 (vs), 725 (vs), 705 (vs), 663 (m) cm^{-1}.

HRMS (EI): m/z for $C_{14}H_{24}OBrSi^+$ $[M-Et]^+$: calcd.: 315.0774
found: 315.0765.

6-*endo*-((*Z*)-2-Bromoalkenyl)-2-*endo*-hydroxybicyclo[2.2.2]octane (500)



499 **500**

To a solution of silylether **499** (524 mg, 1.52 mmol, 1.00 eq.) in THF (18.1 mL) at 0 °C was added TBAF (1 M in THF, 1.82 mL, 1.82 mmol, 1.20 eq.) and the resulting mixture was stirred at room temperature for 40 min. The reaction mixture was extracted with Et_2O (3x 20 mL) and the combined organic layer wwas washed with saturated aqueous NH_4Cl (40 mL), dried (Na_2SO_4) and concentrated *in vacuo*. Purification of the residue by flash column chromatography (3 x 26 cm, silica, hexanes : Et_2O = 8 : 2, 20 mL, #38–61) afforded alkenyl bromide **500** (213 mg, 61%) as a colorless oil.

$C_{10}H_{15}BrO$ M_r = 231.13 g·mol^{-1}.

TLC R_f = 0.12 (hexanes : EtOAc = 9 : 1).

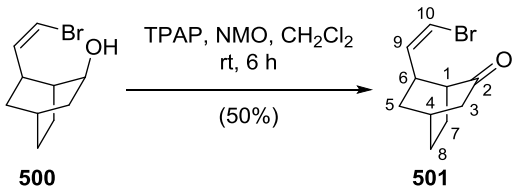
^{1}H NMR (300 MHz, $CDCl_3$): δ = 6.54 (dd, $^3J_{C9\text{-}H,C6\text{-}H}$ = 8.6 Hz, $^3J_{C9\text{-}H,C10\text{-}H}$ = 6.8 Hz, 1H, C9-H), 6.02 (dd, $^3J_{C10\text{-}H,C9\text{-}H}$ = 6.8 Hz, $^4J_{C10\text{-}H,C6\text{-}H}$ = 1.3 Hz, 1H, C10-H), 4.04 (dddd, $^3J_{C2\text{-}H,C3\text{-}Hexo}$ = 9.5 Hz, $^3J_{C2\text{-}H,C3\text{-}Hendo}$ = 3.8 Hz, $^3J_{C2\text{-}H,C1\text{-}H}$ = 2.9 Hz, $^4J_{C2\text{-}H,C6\text{-}H}$ = 1.4 Hz, 1H, C2-H), 2.89 – 2.77 (m, 1H, C6-H), 2.03 – 1.85 (m, 2H, C3-H_A, C5-H_A), 1.84 – 1.78 (m, 1H, C1-H), 1.78 – 1.72 (m, 1H, C4-H), 1.59 – 1.32 (m, 6H, C3-H_B, C5-H_B, C7-H, C8-H) ppm.

^{13}C NMR (75 MHz, $CDCl_3$): δ = 142.6 (C9), 105.3 (C10), 70.5 (C2), 37.7 (C3), 36.6 (C1), 35.7 (C6), 32.9 (C5), 24.5 (C4), 24.5 (C7*), 23.3 (C8*) ppm.

IR (ATR): $\tilde{\nu}$ = 3374 (m), 2954 (vs), 2865 (vs), 1716 (vw), 1614 (w), 1453 (w), 1367 (w), 1350 (w), 1331 (w), 1282 (m), 1158 (vw), 1101 (m), 1057 (w), 1036 (m), 1020 (m), 981 (vw), 948 (w), 921 (vw), 878 (w), 849 (vw), 825 (vw), 796 (vw), 707 (m) cm^{-1}.

HRMS (EI): m/z for $C_{10}H_{13}Br^+$ $[M-H_2O]^+$: calcd.: 212.0201
found: 212.0192

6-*endo*-((*Z*)-2-Bromoalkenyl)-2-oxobicyclo[2.2.2]octane (501)



500 **501**

To a solution of alcohol **500** (150 mg, 0.650 mmol, 1.00 eq.) in CH_2Cl_2 (11.4 mL) was added 4 Å molecular sieves (750 mg), NMO (152 mg, 1.30 mmol, 2.00 eq.) and tetrapropylammonium perruthenate (11.4 mg, 0.030 mmol, 0.050 eq.). The reaction mixture was stirred at room temperature for 6 h, after which time the reaction mixture was concentrated *in vacuo*. The residue was purified by flash column chromatography (3 x 28 cm, silica, *n*-pentane : Et_2O = 9:1, 20 mL, #48─74) to afford ketone **501** (75.0 mg, 50%) as a colorless oil.

$C_{10}H_{13}BrO$ M_r = 229.12 $g \cdot mol^{-1}$.

TLC R_f = 0.24 (hexanes : EtOAc = 9 : 1).

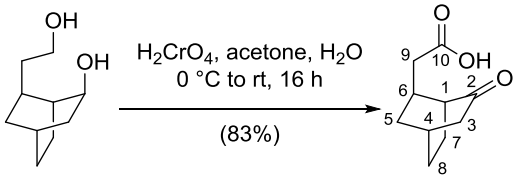
^{1}H NMR (300 MHz, $CDCl_3$): δ = 6.12 (dd, $^3J_{C10\text{-}H,C9\text{-}H}$ = 6.9 Hz, $^3J_{C10\text{-}H,C6\text{-}H}$ = 1.0 Hz, 1H, C10-H), 5.87 (dd, $^3J_{C9\text{-}H,C6\text{-}H}$ = 9.1 Hz, $^3J_{C9\text{-}H,C10\text{-}H}$ = 6.9 Hz, 1H, C9-H), 3.19 – 3.06 (m, 1H, C6-H), 2.36 – 2.10 (m, 6H, C1-H, C3-H, C4-H, C5-H_A), 2.02 – 1.57 (m, 4H, C7-H, C8-H), 1.33 – 1.23 (m, 1H, C5-H_B) ppm.

^{13}C NMR (75 MHz, $CDCl_3$): δ = 216.1 (C2), 138.2 (C9), 107.7 (C10), 47.0 (C1*), 45.1 (C3), 37.1 (C6), 32.5 (C5), 27.8 (C4*), 23.6 (C8), 22.9 (C7) ppm.

IR (ATR): $\tilde{\nu}$ = 3430 (vw), 3056 (vw), 2940 (m), 2869 (w), 1777 (vs), 1591 (w), 1484 (vw), 1438 (m), 1402 (w), 1330 (w), 1194 (m), 1119 (s), 1071 (vw), 1028 (vw), 998 (vw), 868 (vw), 749 (w), 722 (s), 696 (m) cm^{-1}.

HRMS (EI): m/z for $C_{10}H_{13}BrO^+$ $[M]^+$: calcd.: 228.0150
found: 228.0146.

2-(2-Oxobicyclo[2.2.2]octan-6-*endo*-yl)acetic acid (502)



251 **502**

Cold Jones reagent ($Na_2Cr_2O_7 \cdot 2\ H_2O$ (4.36 g, 14.6 mmol, 2.25 eq.) in H_2O (8.00 mL) and concentrated H_2SO_4 (2.78 mL, 52.1 mmol, 8.01 eq.) was added dropwise to a solution of diol **251** (1.10 g, 6.50 mmol, 1.00 eq.) in acetone (26.0 mL) at 0 °C. After the color of the Jones reagent persisted in the reaction mixture it was stirred at room temperature for an additional 16 h. The reaction mixture was quenched with *i*-PrOH and diluted with H_2O (10 mL). The aqueous layer was extracted with Et_2O (3 x 30 mL) and the combined organic layer was washed with H_2O (50 mL), brine (50 mL), dried (Na_2SO_4) and concentrated *in vacuo* to afford keto acid **502** (0.98 g, 83%) as a colorless solid.

$C_{10}H_{14}O_3$ M_r = 182.22 g·mol^{-1}.

TLC R_f = 0.29 (hexanes : EtOAc = 1 : 1).

mp 75 – 77 °C.

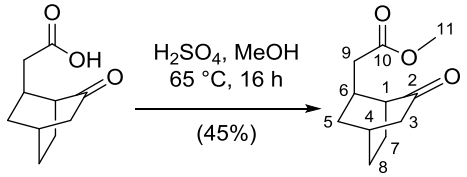
^{1}H NMR (400 MHz, $CDCl_3$): δ = 12.19 – 8.68 (br s, 1H, OH), 2.45 (ddddd, $^3J_{C6\text{-}H,C5\text{-}Hexo}$ = 10.4 Hz, $^3J_{C6\text{-}H,C9\text{-}Ha}$ = 8.5 Hz, $^3J_{C6\text{-}H,C9\text{-}Hb}$ = 6.5 Hz, $^3J_{C6\text{-}H,C5\text{-}Hendo}$ = 6.1 Hz, $^3J_{C6\text{-}H,C1\text{-}H}$ = 2.3 Hz, 1H, C6-H), 2.35 – 2.12 (m, 6H, C1-H, C3-H, C4-H, C9-H), 2.09 (dddd, $^2J_{C5\text{-}Hexo,C5\text{-}Hendo}$ = 13.6 Hz, $^3J_{C5\text{-}Hexo,C6\text{-}H}$ = 10.4 Hz, $^3J_{C5\text{-}Hexo,C4\text{-}H}$ = 2.9 Hz, $^4J_{C5\text{-}Hexo,C3\text{-}Hexo}$ = 2.9 Hz, 1H, C5-H_{exo}), 1.95 – 1.76 (m, 2H, C7-H), 1.74 – 1.57 (m, 2H, C8-H), 1.16 (dddd, $^2J_{C5\text{-}Hendo,C5\text{-}Hexo}$ = 13.6 Hz, $^3J_{C5\text{-}Hendo,C6\text{-}H}$ = 6.1 Hz, $^3J_{C5\text{-}Hendo,C4\text{-}H}$ = 2.4 Hz, $^3J_{C5\text{-}Hendo,C8\text{-}Hsyn}$ = 6.1 Hz, 1H, C5-H_{endo}) ppm.

^{13}C NMR (100 MHz, $CDCl_3$): δ = 216.9 (C2), 177.7 (C10), 47.4 (C1), 44.9 (C3), 41.1 (C9), 33.0 (C5), 32.7 (C6), 28.0 (C4), 23.4 (C8), 23.2 (C7) ppm.

IR (ATR): $\tilde{\nu}$ = 2940 (m), 2871 (w), 1719 (vs), 1402 (w), 1332 (vw), 1228 (w), 1161 (w), 1104 (vw), 915 (vw), 668 (vw) cm^{-1}.

HRMS (ESI–): m/z for $C_{10}H_{13}O_3^-$ $[M–H]^-$: calcd.: 181.0870
found: 181.0870.

Methyl-2-(2-oxobicyclo[2.2.2]octan-6-*endo*-yl)acetate (503)



502 **503**

To a solution of keto acid **502** (0.975 g, 5.35 mmol, 1.00 eq.) in methanol (16.0 mL) was added concentrated H_2SO_4 (0.165 mL) and the resulting mixture was heated to 65 °C for 16 h. The reaction mixture was allowed to cool to room temperature and concentrated *in vacuo*. The residue was dissolved in Et_2O (15 mL) and was washed with saturated aqueous $NaHCO_3$ (10 mL), brine (10 mL), dried (Na_2SO_4) and concentrated *in vacuo*. Purification of the residue by flash column chromatography (4 x 20 cm, silica, hexanes : EtOAc = 3 : 1, 20 mL, #24–39) afforded methyl ester **503** (472 mg, 45%) as a colorless oil.

$C_{11}H_{16}O_3$ M_r = 196.25 g·mol^{-1}.

TLC R_f = 0.47 (hexanes : EtOAc = 1 : 1).

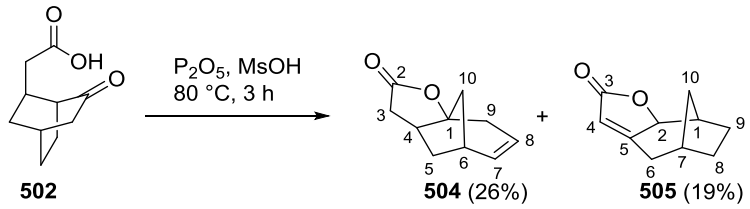
^{1}H NMR (600 MHz, $CDCl_3$): δ = 3.66 (s, 3H, C11-H), 2.46 (ddddd, $^3J_{C6\text{-}H,C5\text{-}Hexo}$ = 10.7 Hz, $^3J_{C6\text{-}H,C9\text{-}H_B}$ = 8.7 Hz, $^3J_{C6\text{-}H,C9\text{-}H_A}$ = 6.8 Hz, $^3J_{C6\text{-}H,C5\text{-}Hendo}$ = 6.4 Hz, $^3J_{C6\text{-}H,C1\text{-}H}$ = 2.3 Hz, 1H, C6-H), 2.28 (dd, $^2J_{C9\text{-}H_A,C9\text{-}H_B}$ = 15.9 Hz, $^3J_{C9\text{-}H_A,C6\text{-}H}$ = 6.8 Hz, 1H, C9-H$_A$), 2.25 (ddd, $^2J_{C3\text{-}Hexo,C3\text{-}Hendo}$ = 18.7 Hz, $^3J_{C3\text{-}Hexo,C4\text{-}H}$ = 2.7 Hz, $^4J_{C3\text{-}Hexo,C5\text{-}Hexo}$ = 2.7 Hz, 1H, C3-H$_{exo}$), 2.19 – 2.11 (m, 4H, C1-H, C3-H$_{endo}$, C4-H, C9-H$_B$), 2.07 (dddd, $^2J_{C5\text{-}Hexo,C5\text{-}Hendo}$ = 13.7 Hz, $^3J_{C5\text{-}Hexo,C6\text{-}H}$ = 10.7 Hz, $^3J_{C5\text{-}Hexo,C4\text{-}H}$ = 3.6 Hz, $^4J_{C5\text{-}Hexo,C3\text{-}Hexo}$ = 2.7 Hz, 1H, C5-H$_{exo}$), 1.88 (dddd, $^2J_{C7\text{-}Hanti,C7\text{-}Hsyn}$ = 14.1 Hz, $^3J_{C7\text{-}Hanti,C8\text{-}Hanti}$ = 11.1 Hz, $^3J_{C7\text{-}Hanti,C8\text{-}Hsyn}$ = 4.5 Hz, $^3J_{C7\text{-}Hanti,C1\text{-}H}$ = 3.1 Hz, 1H, C7-H$_{anti}$), 1.81 (dddd, $^2J_{C7\text{-}Hsyn,C7\text{-}Hanti}$ = 14.1 Hz, $^3J_{C7\text{-}Hsyn,C8\text{-}Hsyn}$ = 11.2 Hz, $^3J_{C7\text{-}Hsyn,C8\text{-}Hanti}$ = 5.7 Hz, $^3J_{C7\text{-}Hsyn,C1\text{-}H}$ = 2.8 Hz, 1H, C7-H$_{syn}$), 1.68 (ddddd, $^2J_{C8\text{-}Hanti,C8\text{-}Hsyn}$ = 13.6 Hz, $^3J_{C8\text{-}Hanti,C7\text{-}Hanti}$ = 11.1 Hz, $^3J_{C8\text{-}Hanti,C7\text{-}Hsyn}$ = 5.7 Hz, $^3J_{C8\text{-}Hanti,C4\text{-}H}$ = 2.6 Hz, $^4J_{C8\text{-}Hanti,C3\text{-}Hendo}$ = 2.6 Hz, 1H, C8-H$_{anti}$), 1.65 – 1.58 (m, 1H, C8-H$_{syn}$), 1.14 (dddd, $^2J_{C5\text{-}Hendo,C5\text{-}Hexo}$ = 13.7 Hz, $^3J_{C5\text{-}Hendo,C6\text{-}H}$ = 6.4 Hz, $^3J_{C5\text{-}Hendo,C4\text{-}H}$ = 2.6 Hz, $^4J_{C5\text{-}Hendo,C8\text{-}Hsyn}$ = 2.6 Hz, 1H, C5-H$_{endo}$) ppm.

^{13}C NMR (150 MHz, $CDCl_3$): δ = 216.4 (C2), 172.6 (C10), 51.7 (C11), 47.6 (C1), 45.0 (C3), 41.2 (C9), 33.1 (C5), 33.0 (C6), 28.0 (C4), 23.5 (C8), 23.3 (C7) ppm.

IR (ATR): $\tilde{\nu}$ = 2940 (w), 2869 (w), 1773 (vw), 1720 (vs), 1454 (w), 1436 (w), 1403 (w), 1373 (w), 1352 (w), 1330 (w), 1311 (w), 1281 (w), 1211 (m), 1158 (s), 1101 (m), 1070 (w), 1063 (w), 1024 (w), 998 (w), 975 (vw), 946 (vw), 926 (vw), 910 (w), 899 (vw), 870 (vw), 837 (w), 813 (vw), 787 (vw) cm^{-1}.

HRMS (EI): m/z for $C_{11}H_{16}O_3^+$ $[M]^+$: calcd.: 196.1094
found: 196.1091.

Cyclization of Keto Acid 502



502 **504** (26%) **505** (19%)

A solution of keto acid **502** (100 mg, 0.550 mmol, 1.00 eq.) in Eaton's reagent (2.00 mL) was heated to 80 °C for 3 h. The reaction mixture was allowed to cool to room temperature and diluted aqueous $NaHCO_3$ was added. The resulting mixture was extracted with Et_2O (3 x 50 mL) and the combined organic layer was washed with saturated aqueous $NaHCO_3$ (2 x 50 mL), H_2O (50 mL), brine (50 mL), dried (Na_2SO_4) and concentrated *in vacuo*. Purification of the residue by flash column chromatography (2 x 15 cm, silica, hexanes : EtOAc = 3 : 1, 8 mL) afforded lactone **504** (#15─19, 23 mg, 26%) and unsaturated lactone **505** (#24─33, 17 mg, 19%) as colorless oils.

*2-Oxatricyclo[5.3.1.0^{1,5}]undec-8-en-3-one (**504**)*

$C_{10}H_{12}O_2$ M_r = 164.20 g·mol^{-1}.

TLC R_f = 0.43 (hexanes : EtOAc = 3 : 1).

^{1}H NMR (400 MHz, $CDCl_3$): δ = 5.91 (ddddd, $^3J_{C7\text{-}H,C8\text{-}H}$ = 9.3 Hz, $^3J_{C7\text{-}H,C6\text{-}H}$ = 6.3 Hz, $^4J_{C7\text{-}H,C9\text{-}H_A}$ = 2.6 Hz, $^4J_{C7\text{-}H,C9\text{-}H_B}$ = 1.4 Hz, $^4J_{C7\text{-}H,C10\text{-}H_B}$ = 1.4 Hz, 1H, C7-H), 5.54 (ddd, $^3J_{C8\text{-}H,C7\text{-}H}$ = 9.3 Hz, $^3J_{C8\text{-}H,C9\text{-}H_B}$ = 4.5 Hz, $^3J_{C8\text{-}H,C9\text{-}H_A}$ = 2.4 Hz, 1H, C8-H), 2.93 – 2.84 (m, 2H, C3-H_A, C9-H_A), 2.68 – 2.62 (m, 1H, C6-H), 2.54 – 2.44 (m, 1H, C4-H), 2.38 – 2.29 (m, 1H, C3-H_B), 2.29 – 2.24 (m, 1H, C5-H_A), 2.24 – 2.17 (m, 1H, C9-H_B), 1.94 (dddd, $^2J_{C10\text{-}H_A,C10\text{-}H_B}$ = 10.7 Hz, $^3J_{C10\text{-}H_A,C6\text{-}H}$ = 2.4 Hz, $^4J_{C10\text{-}H_A,C5\text{-}H_A}$ = 1.1 Hz, $^4J_{C10\text{-}H_A,C9\text{-}H_B}$ = 1.1 Hz, 1H, C10-H_A), 1.81 (dddd, $^2J_{C10\text{-}H_B,C10\text{-}H_A}$ = 10.7 Hz, $^3J_{C10\text{-}H_B,C6\text{-}H}$ = 4.0 Hz, $^4J_{C10\text{-}H_B,C9\text{-}H_B}$ = 1.4 Hz, $^4J_{C10\text{-}H_B,C7\text{-}H}$ = 1.4 Hz, 1H, C10-H_B), 1.66 (ddd, $^2J_{C5\text{-}H_B,C5\text{-}H_A}$ = 12.6 Hz, $^3J_{C5\text{-}H_B,C4\text{-}H}$ = 5.5 Hz, $^3J_{C5\text{-}H_B,C6\text{-}H}$ = 5.5 Hz, 1H, C5-H_B) ppm.

^{13}C NMR (100 MHz, $CDCl_3$): δ = 177.2 (C2), 134.2 (C7), 124.1 (C8), 91.6 (C1), 42.9 (C5), 41.8 (C4), 41.1 (C9), 39.9 (C10), 38.2 (C3), 37.7 (C6) ppm.

IR (ATR): $\tilde{\nu}$ = 2942 (w), 2870 (vw), 1783 (w), 1739 (vs), 1644 (m), 1452 (vw), 1344 (vw), 1315 (vw), 1279 (vw), 1241 (vw), 1212 (vw), 1184 (vw), 1163 (w), 1116 (w), 1070 (vw), 1050 (m), 1012 (vw), 958 (m), 940 (vw), 908 (w), 893 (m), 876 (vw), 852 (w), 832 (vw), 806 (vw), 774 (vw), 732 (vw) cm^{-1}.

HRMS (EI): m/z for $C_{10}H_{12}O_2^+$ $[M]^+$: calcd.: 164.0832
found: 164.0826.

*3-Oxatricyclo[6.2.1.0^{2,6}]undec-5-en-4-one (**505**)*

$C_{10}H_{12}O_2$ M_r = 164.20 g·mol^{-1}.

TLC R_f = 0.25 (hexanes : EtOAc = 3 : 1).

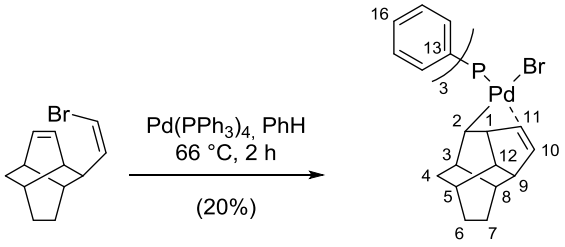
^{1}H NMR (400 MHz, $CDCl_3$): δ = 5.81 (dd, $^4J_{C4\text{-}H,C6\text{-}H_A}$ = 1.8 Hz, $^4J_{C4\text{-}H,C6\text{-}H_B}$ = 1.8 Hz, 1H, C4-H), 4.79 (d, $^3J_{C2\text{-}H,C1\text{-}H}$ = 4.2 Hz, 1H, C2-H), 2.79 – 2.72 (m, 1H, C1-H), 2.59 – 2.37 (m, 3H, C6-H, C7-H), 1.81 (dddd, $^2J_{C10\text{-}H_A,C10\text{-}H_B}$ = 12.7 Hz, $^3J_{C10\text{-}H_A,C1\text{-}H}$ = 5.1 Hz, $^3J_{C10\text{-}H_A,C7\text{-}H}$ = 5.1 Hz, $^4J_{C10\text{-}H_A,C8\text{-}H_B}$ = 2.5 Hz, 1H, C10-H_A), 1.74 – 1.61 (m, 2H, C8-H_A, C10-H_B), 1.47 (ddddd, $^2J_{C9\text{-}H_A,C9\text{-}H_B}$ = 11.5 Hz, $^3J_{C9\text{-}H_A,C8\text{-}H_A}$ = 11.5 Hz, $^3J_{C9\text{-}H_A,C8\text{-}H_B}$ = 6.3 Hz, $^3J_{C9\text{-}H_A,C1\text{-}H}$ = 3.9 Hz, $^4J_{C9\text{-}H_A,C10\text{-}H_B}$ = 1.2 Hz, 1H, C9-H_A), 1.35 – 1.17 (m, 2H, C8-H_B, C9-H_B) ppm.

^{13}C NMR (100 MHz, $CDCl_3$): δ = 174.0 (C3), 169.7 (C5), 116.2 (C4), 84.8 (C2), 40.9 (C1), 36.2 (C10), 36.1 (C6), 35.9 (C7), 28.9 (C8), 22.3 (C9) ppm.

IR (ATR): $\tilde{\nu}$ = 3032 (vw), 2952 (w), 2868 (vw), 2843 (vw), 1777 (vs), 1633 (vw), 1466 (vw), 1449 (vw), 1437 (vw), 1421 (vw), 1337 (vw), 1300 (vw), 1266 (w), 1256 (m), 1224 (w), 1183 (m), 1166 (w), 1133 (w), 1105 (s), 1083 (vs), 1052 (w), 1001 (m), 972 (vw), 939 (vw), 930 (vw), 906 (vw), 881 (vw), 840 (vw), 822 (vw), 764 (vw), 731 (m), 660 (w) cm^{-1}.

HRMS (EI): m/z for $C_{10}H_{12}O_2^+$ $[M]^+$: calcd.: 164.0832
found: 164.0819.

Tetracyclo[7.2.1.0^{3,8}.0^{5,12}]dodec-10-ene-2-yltriphenylphosphinepalladium(II) bromide (512)



463 **512**

To a solution of $Pd(PPh_3)_4$ (243 mg, 0.210 mmol, 1.00 eq.) in benzene (2.33 mL) was added (*Z*)-alkenyl bromide **463** (50.2 mg, 0.210 mmol, 1.00 eq.) by syringe. The yellow reaction mixture was heated to 66 °C for 2 h. The mixture was allowed to cool to room temperature and Et_2O (5 mL) was added, precipitating a white solid. The precipitate was filtered off and the filtrate was allowed to stand. Upon slow evaporation of the solvent palladium complex **512** (25 mg, 20%) crystallized in the form of yellow platelets. Crystals suitable for single crystal X-ray diffraction were obtained from this mixture.

$C_{30}H_{30}BrPPd$ M_r = 607.87 g·mol^{-1}.

TLC R_f = 0.28 (hexanes : EtOAc = 3 : 1).

mp 126 °C (dec.).

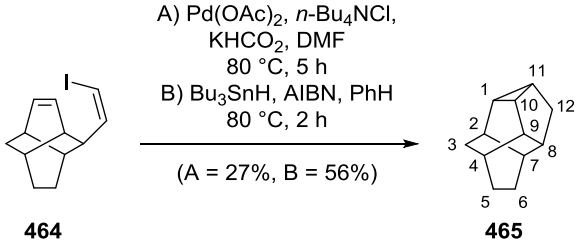
^{1}H NMR (600 MHz, $CDCl_3$): δ = 7.74 – 7.68 (m, 6H, C14-H), 7.46 – 7.37 (m, 9H, C15-H, C16-H), 6.77 – 6.68 (m, 1H, C10-H), 6.08 – 6.01 (m, 1H, C11-H), 3.21 – 3.13 (m, 1H, C1-H), 2.70 – 2.63 (m, 1H, C8-H), 2.42 – 2.35 (m, 1H, C12-H), 2.25 – 2.18 (m, 1H, C9-H), 1.78 – 1.71 (m, 1H, C5-H), 1.55 – 1.41 (m, 4H, C6-H, C7-H), 1.31 – 1.25 (m, 1H, C3-H), 1.19 – 1.12 (m, 1H, C4-H_A), 1.01 – 0.92 (m, 1H, C2-H), 0.83 – 0.76 (m, 1H, C4-H_B) ppm.

^{13}C NMR (150 MHz, $CDCl_3$): δ = 134.8 (d, $^2J_{C14,P}$ = 12.4 Hz, C14), 131.1 (d, $^1J_{C13,P}$ = 42.4 Hz, C13), 130.6 (s, C16), 128.5 (d, $^3J_{C15,P}$ = 10.4 Hz, C15), 121.5 (br s, C10), 89.3 (br s, C11), 50.7 (s, C12), 46.1 (s, C9), 45.8 (s, C1), 36.0 (s, C3), 35.7 (s, C8), 33.4 (br s, C4), 25.6 (s, C5), 25.1 (s, C10), 24.7 (d, $^2J_{C2,P}$ = 6.9 Hz, C2), 24.2 (s, C9) ppm.

IR (ATR): $\tilde{\nu}$ = 3053 (vw), 2918 (w), 2865 (w), 2213 (vw), 1899 (vw), 1818 (vw), 1616 (vw), 1587 (vw), 1573 (vw), 1481 (w), 1456 (vw), 1435 (m), 1388 (vw), 1339 (vw), 1328 (vw), 1321 (vw), 1301 (vw), 1286 (vw), 1266 (vw), 1240 (vw), 1222 (vw), 1184 (w), 1159 (vw), 1140 (vw), 1119 (vw), 1095 (m), 1082 (vw), 1071 (vw), 1062 (vw), 1049 (vw), 1028 (vw), 1017 (vw), 999 (w), 907 (s), 880 (vw), 868 (vw), 850 (vw), 823 (vw), 791 (vw), 724 (vs), 691 (vs) cm^{-1}.

HRMS (ESI+): m/z for $C_{30}H_{30}PPd^+$ $[M–Br]^+$: calcd.: 527.1114
found: 527.1115.

Pentacyclo[6.2.2.0^{2,7}.0^{4,9}.0^{10,11}]dodecane (465)



464 **465**

Method A:

To a round bottom flask were added $Pd(OAc)_2$ (0.6 mg, 2.50 µmol, 0.025 eq.), *n*-Bu_4NCl (27.8 mg, 100 µmol, 1.00 eq.) and potassium formate (25.2 mg, 300 µmol, 3.00 eq.). The flask was evacuated and refilled with argon three times. The salts were dissolved in degassed DMF (10.0 mL) and alkenyl iodide **464** (28.6 mg, 100 µmol, 1.00 eq.) was added. The reaction mixture was transferred to a preheated oil bath and stirred at 80 °C for 5 h. During the reaction the color of the mixture turned from yellow to black. The reaction mixture was allowed to cool to room temperature and was diluted with H_2O (25 mL) and pentane (25 mL) and the resulting mixture was stirred for 15 min at room

temperature. The organic layer was separated and the aqueous layer was extracted with *n*-pentane (3 x 25 mL). The combined organic layer was dried (Na_2SO_4) and concentrated *in vacuo* (at room temperature). Purification of the residue by flash column chromatography (1 x 15 cm, silica, *n*-pentane, 8 mL, #8) afforded cyclopropane **465** (4.3 mg, 27%) as a colorless waxy solid.

Method B:

To a solution of (*Z*)-alkenyl iodide **464** (25.8 mg, 90.0 µmol, 1.00 eq.) and a crystal of AIBN in refluxing benzene (2.00 mL) was added dropwise a solution of Bu_3SnH (40 µL, 43 mg, 148 µmol, 1.70 eq.) and AIBN (1.5 mg, 9.00 µmol, 0.100 eq.) in benzene (8.00 mL). The resulting mixture was heated to 80 °C for 2 h and was then allowed to cool to room temperature. The solvent was removed *in vacuo* and the residue was purified by flash column chromatography (2 x 16 cm, silica, *n*-pentane, 8 mL, #6–7) to afford cyclopropane **465** (8.0 mg, 56%) as a colorless waxy solid.

$C_{12}H_{16}$ M_r = 160.26 g·mol^{-1}.

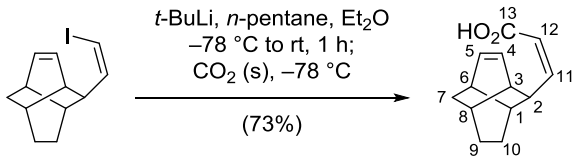
TLC R_f = 0.82 (hexanes).

^{1}H NMR (600 MHz, $CDCl_3$): δ = 2.19 – 2.12 (m, 1H, C9-H), 2.02 – 1.97 (m, 1H, C2-H), 1.85 – 1.80 (m, 1H, C4-H), 1.75 (dddd, $^2J_{C12\text{-}H_A,C12\text{-}H_B}$ = 11.4 Hz, $^3J_{C12\text{-}H_A,C8\text{-}H}$ = 6.1 Hz, $^3J_{C12\text{-}H_A,C11\text{-}H}$ = 3.1 Hz, $^4J_{C12\text{-}H_A,C1\text{-}H}$ = 0.9 Hz, 1H, C12-H_A), 1.65 – 1.60 (m, 1H, C8-H), 1.55 – 1.52 (m, 1H, C12-H_B), 1.52 – 1.48 (m, 3H, C5-H, C6-H_A), 1.42 – 1.38 (m, 2H, C3-H_A, C11-H), 1.36 – 1.32 (m, 1H, C3-H_B), 1.30 – 1.25 (m, 1H, C6-H_B), 1.21 – 1.18 (m, 1H, C7-H), 1.18 – 1.15 (m, 1H, C10-H), 0.87 – 0.83 (m, 1H, C1-H) ppm.

^{13}C NMR (150 MHz, $CDCl_3$): δ = 38.2 (C9), 37.4 (C8), 34.1 (C7), 32.9 (C12), 31.2 (C3), 28.3 (C2), 26.1 (C5), 26.0 (C4), 23.5 (C6), 22.5 (C11), 18.8 (C1), 16.8 (C10) ppm.

HRMS (EI): m/z for $C_{12}H_{16}^+$ $[M]^+$: calcd.: 160.1247
found: 160.1249.

2((*Z*)-2-Carboxyalkenyl)tricyclo[4.4.0.0^{3,8}]dec-4-ene (515)



464 **515**

To a solution of alkenyl iodide **464** (28.6 mg, 0.100 mmol, 1.00 eq.) in *n*-pentane : Et_2O (3 : 2, 1.00 mL) at –78 °C was added a solution of *t*-BuLi in *n*-pentane (1.7 M, 0.129 mL, 0.220 mmol, 2.20 eq.) over 5 min. The mixture was stirred at –78 °C for 5 min and was then allowed to warm to room temperature. After stirring at room temperature for an additional 1 h, the mixture was recooled to –78 °C and an excess of solid CO_2 was added. The reaction mixture was stirred for another 5 min at –78 °C and was then warmed to room temperature and stirred at room temperature for an additional

30 min. The mixture was diluted with H_2O (5 mL) and 10% aqueous NaOH (5 mL). The aqueous layer was washed with Et_2O (2 x 5 mL) and acidified with HCl, followed by extraction with Et_2O (5 x 10 mL). The combined organic layer was washed with H_2O (20 mL), brine (20 mL), dried (Na_2SO_4) and concentrated *in vacuo* to afford alkenyl carboxylic acid **515** (15 mg, 73%) as a colorless solid.

$C_{13}H_{16}O_2$ $M_r = 204.27\ g{\cdot}mol^{-1}$.

TLC $R_f = 0.69$ (hexanes : EtOAc = 1 : 1).

mp 84 – 96 °C.

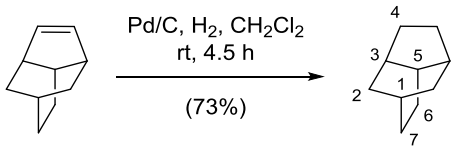
^{1}H NMR (600 MHz, $CDCl_3$): δ = 6.52 (ddd, $^3J_{C5\text{-}H,C4\text{-}H} = 7.8$ Hz, $^3J_{C5\text{-}H,C6\text{-}H} = 6.2$ Hz, $^4J_{C5\text{-}H,C3\text{-}H} = 1.5$ Hz, 1H, C5-H), 6.27 (dd, $^3J_{C11\text{-}H,C12\text{-}H} = 11.6$ Hz, $^3J_{C11\text{-}H,C2\text{-}H} = 8.3$ Hz, 1H, C11-H), 5.95 (ddd, $^3J_{C4\text{-}H,C5\text{-}H} = 7.8$ Hz, $^3J_{C4\text{-}H,C3\text{-}H} = 6.0$ Hz, $^3J_{C4\text{-}H,C6\text{-}H} = 1.4$ Hz, 1H, C4-H), 5.63 (dd, $^3J_{C12\text{-}H,C11\text{-}H} = 11.6$ Hz, $^4J_{C12\text{-}H,C2\text{-}H} = 1.5$ Hz, 1H, C12-H), 3.81 – 3.76 (m, 1H, C2-H), 2.95 – 2.90 (m, 1H, C3-H), 2.63 – 2.58 (m, 1H, C6-H), 1.90 – 1.82 (m, 1H, C9-H_A), 1.77 – 1.65 (m, 3H, C7-H_A, C10-H), 1.62 – 1.55 (m, 2H, C8-H, C9-H_B), 1.50 – 1.46 (m, 1H, C1-H), 1.02 (m, 1H, C7-H_B) ppm.

^{13}C NMR (150 MHz, $CDCl_3$): δ = 171.8 (C13), 159.8 (C11), 138.0 (C5), 130.3 (C4), 116.8 (C12), 43.2 (C2), 39.0 (C3), 36.9 (C7), 34.6 (C6), 32.4 (C1), 25.1 (C9), 25.0 (C10), 23.9 (C8) ppm.

IR (ATR): $\tilde{\nu}$ = 3042 (w), 2935 (s), 2874 (m), 2737 (vw), 2575 (vw), 1686 (vs), 1626 (s), 1481 (vw), 1438 (m), 1378 (vw), 1360 (w), 1297 (w), 1244 (s), 1222 (vs), 1204 (s), 1169 (m), 1137 (w), 1117 (w), 1070 (w), 1055 (vw), 1024 (vw), 1006 (vw), 926 (m), 890 (w), 880 (w), 858 (m), 848 (w), 826 (s), 809 (w), 792 (m), 746 (w), 720 (vw), 682 (s), 665 (vw) cm^{-1}.

HRMS (EI): m/z for $C_{13}H_{16}O_2^+$ $[M]^+$: calcd.: 204.1145
found: 204.1143.

Tricyclo[4.3.1.0^{3,7}]decane – Isotwistane (544)



426 **544**

To a solution of isotwistene (**426**) (101 mg, 0.750 mmol, 1.00 eq.) in CH_2Cl_2 (45 mL) was added Pd on activated charcoal (10 wt-% Pd, 8.0 mg, 7.50 µmol, 0.010 eq.) and the resulting mixture was treated with hydrogen by three turns of evacuating and flushing with hydrogen. The mixture was stirred at room temperature for 4.5 h, after which time the catalyst was filtered off over celite. The

residue was washed with CH_2Cl_2 (10 mL) and the combined filtrate was concentrated *in vacuo* at room temperature to afford isotwistane (**544**) (75 mg, 73%) as a waxy colorless solid.

$C_{10}H_{16}$ M_r = 136.24 g·mol^{-1}.

TLC R_f = 0.82 (hexanes).

mp 85 – 87 °C.

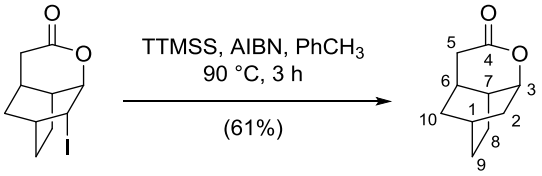
^{1}H NMR (600 MHz, $CDCl_3$): δ = 1.99 – 1.92 (m, 2H, C3-H), 1.83 – 1.74 (m, 4H, C2-H_A, C4-H_A), 1.72 – 1.66 (m, 2H, C6-H), 1.48 – 1.45 (m, 1H, C1-H), 1.40 – 1.34 (m, 3H, C5-H, C7-H), 1.33 – 1.28 (m, 2H, C4-H_B), 1.15 – 1.10 (m, 2H, C2-H_B) ppm.

^{13}C NMR (150 MHz, $CDCl_3$): δ = 37.5 (C2), 36.5 (C5), 35.3 (C3), 34.1 (C4), 26.8 (C7), 23.2 (C1), 19.4 (C6) ppm.

IR (ATR): $\tilde{\nu}$ = 3393 (vw), 2921 (vs), 2849 (m), 1644 (w), 1462 (vw), 1377 (vw) cm^{-1}.

HRMS (EI): m/z for $C_{10}H_{16}^+$ $[M]^+$: calcd.: 136.1247
found: 136.1246.

4-Oxatricyclo[5.3.1.0^{3,8}]undecan-5-one (250)



249 **250**

To a solution of iodolactone **249** (152 mg, 0.520 mmol, 1.00 eq.) in toluene (15.6 mL) was added TTMSS (0.241 mL, 194 mg, 0.780 mmol, 1.50 eq.) and AIBN (12.8 mg, 0.078 mmol, 0.150 eq.). The resulting mixture was heated to 90 °C for 3 h and was then allowed to cool to room temperature and was concentrated *in vacuo*. The residue was purified by flash column chromatography (3 x 10 cm, silica, *n*-pentane : EtOAc = 3 : 1, 20 mL, #14–32) to afford lactone **250** (53 mg, 61%) as a colorless solid.

$C_{10}H_{14}O_2$ M_r = 166.22 g·mol^{-1}.

TLC R_f = 0.31 (hexanes : EtOAc = 3 : 1).

mp 66 – 68 °C.

^{1}H NMR (400 MHz, $CDCl_3$): δ = 4.65 – 4.57 (m, 1H, C3-H), 2.54 (dd, $^2J_{C5\text{-}HA,C5\text{-}HB}$ = 18.0 Hz, $^3J_{C5\text{-}HA,C6\text{-}H}$ = 5.2 Hz, 1H, C5-H_A), 2.45 (dd, $^2J_{C5\text{-}HB,C5\text{-}HA}$ = 18.0 Hz, $^3J_{C5\text{-}HB,C6\text{-}H}$ = 2.1 Hz, 1H, C5-H_B), 2.12 – 2.00 (m, 1H, C6-H), 1.99 – 1.88 (m, 2H, C2-H_A, C10-H_{anti}), 1.85 (dddd, $^3J_{C7\text{-}H,C3\text{-}H}$ = 4.7 Hz, $^3J_{C7\text{-}H,C8\text{-}Hexo}$ = 4.7 Hz, $^3J_{C7\text{-}H,C6\text{-}H}$ = 2.4 Hz, $^3J_{C7\text{-}H,C8\text{-}Hendo}$ = 2.4 Hz, 1H, C7-H), 1.77 – 1.65 (m, 3H, C1-H, C2-H_B, C8-H_{exo}), 1.55 – 1.44 (m, 1H, C8-H_{endo}), 1.43 – 1.32 (m, 2H, C9-H), 1.21 (dddd,

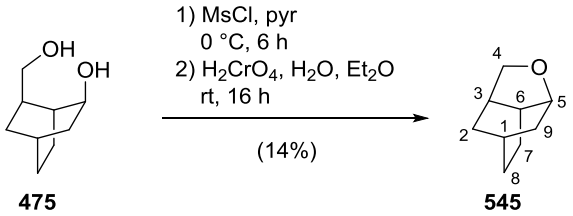
$^{2}J_{C10\text{-}Hsyn,C10\text{-}Hanti}$ = 13.4 Hz, $^{3}J_{C10\text{-}Hsyn,C6\text{-}H}$ = 5.7 Hz, $^{3}J_{C10\text{-}Hsyn,C1\text{-}H}$ = 3.0 Hz, $^{4}J_{C10\text{-}Hsyn,C9\text{-}Hendo}$ = 1.6 Hz, 1H, C10-H_{syn}) ppm.

^{13}C NMR (100 MHz, $CDCl_3$): δ = 170.6 (C4), 77.9 (C3), 39.6 (C5), 35.8 (C2), 33.2 (C10), 28.8 (C7), 26.0 (C6), 23.3 (C9), 22.9 (C1), 20.9 (C8) ppm.

IR (ATR): $\tilde{\nu}$ = 2932 (m), 2863 (w), 1726 (vs), 1455 (vw), 1385 (w), 1368 (w), 1356 (w), 1258 (vw), 1223 (m), 1181 (m), 1164 (w), 1099 (w), 1087 (w), 1054 (m), 1012 (m), 970 (vw), 952 (vw), 837 (vw), 746 (vw) cm^{-1}.

HRMS (EI): m/z for $C_{10}H_{14}O_2^+$ $[M]^+$: calcd.: 166.0988
found: 166.0986

5-Oxatricyclo[4.3.1.0^{3,7}]decane (545)



475 **545**

To a solution of diol **475** (200 mg, 1.28 mmol, 1.00 eq.) in pyridine (2.00 mL) at 0 °C was added dropwise MsCl (0.109 mL, 161 mg, 1.41 mmol, 1.10 eq.). The mixture was allowed to stand at 0 °C for 6 h, then 0.4 mL H_2O were added and the resulting solution was stirred at 0 °C for 0.5 h. The reaction mixture was poured into a mixture of ice and 1 M HCl (10 mL) and the aqueous layer was extracted with Et_2O (5 x 10 mL). The organic layer was washed with water (20 mL), brine (20 mL), dried (Na_2SO_4) and concentrated *in vacuo* to about 4 mL. To this solution containing the crude mesylate was added a mixture of sodium dichromate dihydrate (160 mg, 0.537 mmol, 0.419 eq.) in H_2O (0.8 mL) and H_2SO_4 (0.12 mL, 2.25 mmol, 1.76 eq.). The resulting mixture was stirred at room temperature for 16 h and was then poured into water (5 mL) and extracted with Et_2O (3 x 5 mL). The combined organic layer was washed with water (2 x 7.5 mL), brine (2 x 7.5 mL), dried (Na_2SO_4) and concentrated *in vacuo*. Purification of the residue by flash column chromatography (2 x 13 cm, silica, *n*-pentane : Et_2O = 2 : 1 to 1 : 1, 8 mL, #11–13) afforded tricyclic ether **545** (25 mg, 14%) as a colorless solid.

$C_9H_{14}O$ M_r = 138.21 g·mol^{-1}.

TLC R_f = 0.82 (hexanes : EtOAc = 1 : 1).

mp 145 – 148 °C.

^{1}H NMR (600 MHz, $CDCl_3$): δ = 4.10 (dd, $^{3}J_{C5\text{-}H,C9\text{-}HA}$ = 6.2 Hz, $^{3}J_{C5\text{-}H,C6\text{-}H}$ = 6.2 Hz, 1H, C5-H), 3.75 (dd, $^{2}J_{C4\text{-}HA,C4\text{-}HB}$ = 7.4 Hz, $^{3}J_{C4\text{-}HA,C3\text{-}H}$ = 4.0 Hz, 1H, C4-H_A), 3.46 (d, $^{2}J_{C4\text{-}HB,C4\text{-}HA}$ = 7.4 Hz, 1H, C4-H_B), 2.17 (dddd, $^{3}J_{C3\text{-}H,C2\text{-}HA}$ = 9.7 Hz, $^{3}J_{C3\text{-}H,C4\text{-}HA}$ = 4.0 Hz, $^{3}J_{C3\text{-}H,C6\text{-}H}$ = 4.0 Hz, $^{3}J_{C3\text{-}H,C2\text{-}HB}$ = 1.5 Hz, 1H, C3-H), 1.92 – 1.88

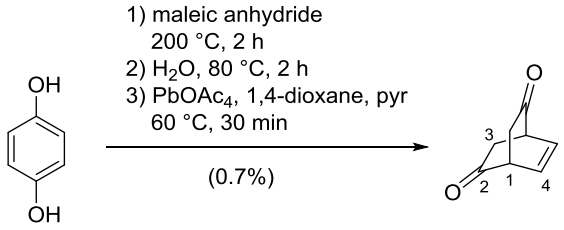
(m, 1H, C6-H), 1.87 – 1.81 (m, 1H, C2-H_A), 1.78 (dddd, $^2J_{C7\text{-}HA,C7\text{-}HB}$ = 14.3 Hz, $^3J_{C7\text{-}HA,C8\text{-}HA}$ = 10.6 Hz, $^3J_{C7\text{-}HA,C8\text{-}HB}$ = 5.1 Hz, $^3J_{C7\text{-}HA,C6\text{-}H}$ = 3.6 Hz, 1H, C7-H_A), 1.67 – 1.62 (m, 2H, C7-H_B, C9-H_A), 1.62 – 1.59 (m, 1H, C1-H), 1.51 (ddd, $^2J_{C9\text{-}HB,C9\text{-}HA}$ = 14.2 Hz, $^3J_{C9\text{-}HB,C1\text{-}H}$ = 4.4 Hz, $^3J_{C9\text{-}HB,C6\text{-}H}$ = 2.4 Hz, 1H, C9-H_B), 1.43 – 1.40 (m, 1H, C2-H_B), 1.40 – 1.33 (m, 2H, C8-H) ppm.

^{13}C NMR (150 MHz, $CDCl_3$): δ = 76.3 (C4), 75.7 (C5), 38.0 (C9), 35.2 (C2), 35.0 (C6), 34.9 (C3), 26.3 (C8), 22.0 (C1), 16.2 (C7) ppm.

IR (ATR): $\tilde{\nu}$ = 2929 (vs), 2862 (s), 1470 (vw), 1451 (vw), 1434 (vw), 1342 (vw), 1282 (vw), 1154 (vw), 1102 (w), 1073 (s), 1050 (w), 996 (vs), 962 (m), 942 (m), 881 (w), 853 (m), 820 (vw), 753 (s), 710 (vw), 668 (vw) cm^{-1}.

HRMS (EI): m/z for $C_9H_{14}O^+$ $[M]^+$: calcd.: 138.1039
found: 138.1038.

Bicyclo[2.2.2]oct-7-ene-2,5-dione (547)



546 **547**

A mixture of hydroquinone (**546**) (33.0 g, 300 mmol, 1.00 eq.) and maleic anhydride (58.8 g, 600 mmol, 2.00 eq.) was heated to 200 °C for 2 h. The mixture was allowed to cool to 70 °C and then carefully poured into Et_2O (160 mL). The restulting mixture was left to stand and the resulting solid was filtered off and washed with Et_2O to afford bicyclic anhydride (2.18 g, 4%) as brown crystals, which were used in the next step without further purification.

The crude material from the previous step (2.18 g, 10.4 mmol, 1.00 eq.) was dissolved in water (25.0 mL) and the solution was heated to 80 °C for 2 h. The mixture was allowed to cool to room temperature and subsequently cooled to 4 °C for 20 h. The resulting precipitate was collected by filtration was used in the next step without further purification.

A mixture of the crude product (1.58 g, 7.00 mmol, 1.00 eq.) and lead tetraacetate (6.21 g, 14.0 mmol, 2.00 eq.) in dioxane (14.0 mL) was degassed by bubbling argon through the mixture for 15 min. To this reaction mixture was added pyridine (14.0 mL, 13.7 g, 173 mmol, 24.7 eq.) over a period of 10 min and the resulting mixture was heated to 60 °C for 30 min. The mixture was allowed to cool to room temperature and poured into 3 N HNO_3 (85 mL). The mixture was extracted with CH_2Cl_2 (8 x 10 mL) and the combined organic layer was washed with H_2O (50 mL), 5 wt-% aqueous $NaHCO_3$ (50 mL), brine (50 mL), dried (Na_2SO_4) and concentrated *in vacuo*. Purification of the residue by flash

column chromatography (3 x 25 cm, silica, hexanes : EtOAc = 9 : 1 to 3 : 2, 20 mL, #86─115) afforded bicyclooctenedione **547** (217 mg, 23%) as a colorless solid.

$C_8H_8O_2$ M_r = 136.15 g·mol^{-1}.

TLC R_f = 0.21 (hexanes : EtOAc = 3 : 1).

mp 96 – 99 °C.

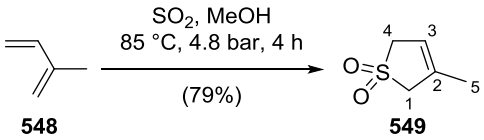
^{1}H NMR (600 MHz, $CDCl_3$): δ = 6.53 – 6.50 (m, 2H, C4-H), 3.46 – 3.40 (m, 2H, C1-H), 2.40 (dd, $^2J_{C3\text{-}H_A,C3\text{-}H_B}$ = 18.6 Hz, $^3J_{C3\text{-}H_A,C1\text{-}H}$ = 2.3 Hz, 1H, C3-H_A), 2.32 (dd, $^2J_{C3\text{-}H_B,C3\text{-}H_A}$ = 18.6 Hz, $^3J_{C3\text{-}Hb,C1\text{-}H}$ = 3.2 Hz, 1H, C3-H_B) ppm.

^{13}C NMR (150 MHz, $CDCl_3$): δ = 207.6 (C2), 132.2 (C4), 50.0 (C1), 35.1 (C3) ppm.

IR (ATR): $\tilde{\nu}$ = 3438 (vw), 3064 (vw), 2979 (vw), 2916 (vw), 2250 (vw), 1725 (vs), 1606 (vw), 1403 (w), 1345 (vw), 1304 (vw), 1255 (vw), 1223 (vw), 1189 (vw), 1152 (vw), 1124 (vw), 1090 (w), 1066 (m), 1025 (vw), 975 (vw), 949 (m), 917 (vw), 893 (m), 882 (w), 757 (m), 732 (vw), 683 (s) cm^{-1}.

HRMS (EI): m/z for $C_8H_8O_2^+$ $[M]^+$: calcd.: 136.0519
found: 136.0519.

2,5-Dihydro-3-methylthiophene-1,1-dioxide (549)



548 **549**

An autoclave was charged with a solution of isoprene (**548**) (44.1 mL, 30.0 g, 440 mmol, 1.00 eq.) and hydroquinone (**546**) (1.00 g, 9.08 mmol, 0.020 eq.) in MeOH (22.0 mL). Dry-ice condensed SO_2 (19.3 mL, 28.2 g, 440 mmol, 1.00 eq.) was transferred by cannula to the mixture in the autoclave, the vessel was sealed and slowly heated to 85 °C resulting in a pressure of 4.8 bar. At these conditions, the reaction mixture was stirred for 4 h and was then allowed to cool to room temperature. The reaction mixture was transferred to a round bottom flask and the autoclave was rinsed with MeOH. The solvent was removed *in vacuo* and purification of the residue by flash column chromatography (15 x 25 cm, silica, hexanes : EtOAc = 3 : 2, 100 mL, #71─158) afforded sulfolene **549** (46.0 g, 79%) as a colorless solid.

$C_5H_8O_2S$ M_r = 132.18 g·mol^{-1}.

TLC R_f = 0.35 (hexanes : EtOAc = 1 : 1).

mp 65 – 68 °C.

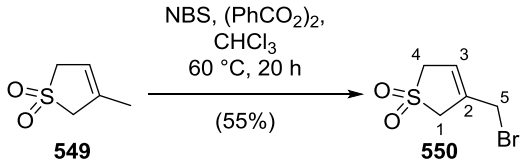
^{1}H NMR (300 MHz, $CDCl_3$): δ = 5.70 – 5.60 (m, 1H, C3-H), 3.78 – 3.73 (m, 2H, C4-H), 3.67 – 3.62 (m, 2H, C1-H), 1.86 – 1.83 (m, 3H, C5-H) ppm.

^{13}C NMR (75 MHz, $CDCl_3$): δ = 134.3 (C2), 118.0 (C3), 59.0 (C1), 57.4 (C4), 18.9 (C5) ppm.

IR (ATR): $\tilde{\nu}$ = 3060 (vw), 2963 (w), 2921 (vw), 2359 (vw), 2255 (vw), 1653 (vw), 1436 (w), 1413 (w), 1380 (w), 1301 (s), 1283 (s), 1265 (s), 1248 (vs), 1154 (s), 1112 (vs), 1037 (m), 962 (vw), 929 (w), 898 (s), 852 (vw), 788 (vs), 729 (vs), 706 (m), 668 (vw) cm^{-1}.

HRMS (EI): m/z for $C_5H_8O_2S^+$ $[M]^+$: calcd.: 132.0240
found: 132.0236.

3-Bromomethyl-2,5-dihydrothiophene-1,1-dioxide (550)



A solution of sulfolene **549** (40.4 g, 305 mmol, 1.00 eq.), NBS (54.3 g, 305 mmol, 1.00 eq.) and benzoyl peroxide (3.69 g, 15.3 mmol, 0.050 eq.) in $CHCl_3$ (500 mL) was stirred at 75 °C for 20 h. The solution was allowed to cool to room temperature and the mixture was concentrated *in vacuo* to a volume of about 350 mL and filtered to remove precipitated succinimide. The filtrate was concentrated to dryness *in vacuo* and the residue was submitted to flash column chromatography (15 x 20 cm, silica, hexanes : EtOAc = 2 : 1 to 3 : 2, 100 mL, #53─100) to afford bromosulfolene **550** (35.5 g, 55%) as a colorless solid.

$C_5H_7BrO_2S$ M_r = 211.08 $g \cdot mol^{-1}$.

TLC R_f = 0.50 (hexanes : EtOAc = 1 : 1).

mp 76 – 78 °C.

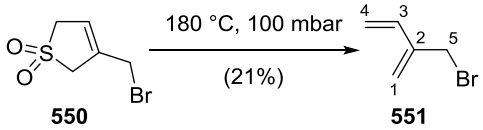
^{1}H NMR (400 MHz, $CDCl_3$): δ = 6.09 (m, 1H, C3-H), 4.03 (m, 2H, C5-H), 3.88 (m, 4H, C1-H, C4-H) ppm.

^{13}C NMR (100 MHz, $CDCl_3$): δ = 134.5 (C2), 122.3 (C3), 57.5 (C1), 56.7 (C4), 29.8 (C5) ppm.

IR (ATR): $\tilde{\nu}$ = 3024 (vw), 2979 (vw), 2938 (vw), 1722 (vw), 1640 (vw), 1428 (vw), 1406 (vw), 1392 (m), 1301 (vs), 1254 (m), 1238 (vs), 1214 (s), 1156 (s), 1131 (vs), 1108 (vs), 1098 (vs), 1034 (w), 1001 (m), 921 (w), 910 (m), 893 (w), 861 (vw), 801 (m), 793 (vs), 710 (vw) cm^{-1}.

HRMS (EI): m/z for $C_5H_7BrO_2S^+$ $[M]^+$: calcd.: 209.9345
found: 209.9331.

2-Bromomethylbuta-1,3-diene (551)



Brominosulfolene **550** (500 mg, 2.37 mmol, 1.00 eq.) was placed in a short-path distillation apparatus and pyrolyzed at a vacuum of 100 mbar and an oil-bath temperature of 180 °C. Bromodiene **551** (72 mg, 21 %) was collected as colorless oil in a dry-ice cooled receiver flask as the fraction that boiled at 45 °C. The product was used in the next step without further purification.

C_5H_7Br M_r = 147.01 g·mol^{-1}.

TLC R_f = 0. 89 (hexanes).

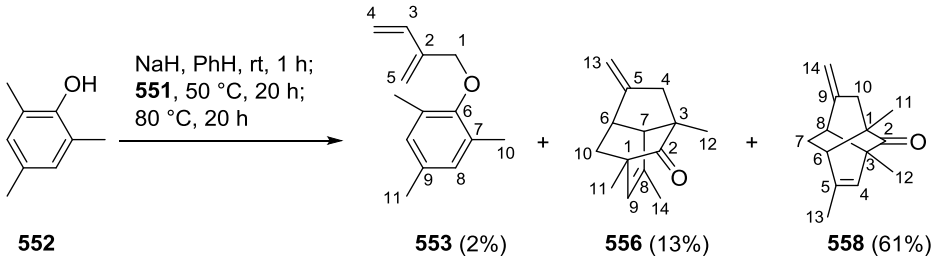
^{1}H NMR (300 MHz, $CDCl_3$): δ = 6.46 – 6.24 (m, 1H, C3-H), 5.48 – 5.21 (m, 4H, C1-H, C4-H), 4.13 – 4.07 (m, 2H, C5-H) ppm.

^{13}C NMR (75 MHz, $CDCl_3$): δ = 142.6 (C2), 135.2 (C3), 120.3 (C1), 116.1 (C4), 30.7 (C5) ppm.

IR (ATR): $\tilde{\nu}$ = 3091 (vw), 2974 (vw), 2925 (vw), 2854 (vw), 1830 (vw), 1718 (vw), 1695 (vw), 1591 (vw), 1452 (vw), 1427 (vw), 1390 (vw), 1316 (m), 1239 (w), 1212 (s), 1153 (vw), 1126 (w), 1071 (vw), 1043 (vw), 990 (w), 966 (vw), 909 (vs), 791 (vw), 713 (w), 668 (vw), 609 (w) cm^{-1}.

HRMS (EI): m/z for $C_5H_7Br^+$ $[M]^+$: calcd.: 145.9726
found: 145.9743.

Allylation/Claisen/Diels-Alder Cascade of Mesitol (552)



To a suspension of NaH (3.01 g, 125 mmol, 3.67 eq.) in benzene (50.0 mL) was added slowly a solution of mesitol (**552**) (16.3 g, 119 mmol, 3.50 eq.) in benzene (125 mL). After complete addition, the reaction mixture was stirred at room temperature for 1 h. Then, freshly distilled bromodiene **551** (3.72 mL, 5.02 g, 34.1 mmol, 1.00 eq.) was added and the resulting reaction mixture was stirred at 50 °C for 20 h, after which time the reaction mixture was heated to 80 °C and stirred at this temperature for an additional 20 h. The reaction mixture was allowed to cool to room temperature, H_2O (250 mL) was added and the mixture was extracted with *n*-pentane (5 x 100 mL). The combined organic layers were washed with 10 wt-% aqueous NaOH (150 mL), Claisen lye (100 mL), H_2O

(150 mL), dried (Na_2SO_4) and concentrated *in vacuo*. Purification of the residue by flash column chromatography (5 x 25 cm, silica, *n*-pentane : Et_2O = gradient from 99 : 1 to 95 : 1, 100 mL) afforded mesitylether **553** (0.114 g, 2%, #13─14) as a colorless oil, isotwistene **556** (0.915 g, 13%, #17─19) as a colorless oil and twistene **558** (4.22 g, 61%, #21─35) as a colorless solid. Recrystallization of twistene **558** from hexanes afforded crystals suitable for single crystal X-ray diffraction.

*2-Methylen-3-butenylmesitylether (**553**)*

$C_{14}H_{18}O$ M_r = 202.29 g·mol^{-1}.

TLC R_f = 0.71 (hexanes : EtOAc = 9 : 1).

^{1}H NMR (300 MHz, $CDCl_3$): δ = 6.86 – 6.83 (m, 2H, C8-H), 6.54 – 6.41 (m, 1H, C3-H), 5.56 – 5.53 (m, 1H, C5-H_A), 5.32 – 5.25 (m, 2H, C4-H_A, C5-H_B), 5.17 – 5.10 (m, 1H, C4-H_B), 4.48 – 4.42 (m, 2H, C1-H), 2.28 – 2.25 (2s, 9H, C10-H, C11-H) ppm.

^{13}C NMR (75 MHz, $CDCl_3$): δ = 154.0 (C2), 142.5 (C6), 136.8 (C3), 133.3 (C9), 130.8 (C7), 129.5 (C8), 116.9 (C5), 113.9 (C4), 71.4 (C1), 20.8 (C11), 16.4 (C10) ppm.

IR (ATR): $\tilde{\nu}$ = 3086 (vw), 2918 (w), 2859 (vw), 1817 (vw), 1720 (vw), 1639 (vw), 1597 (w), 1483 (m), 1460 (w), 1391 (vw), 1374 (w), 1307 (w), 1211 (vs), 1148 (s), 1069 (w), 1017 (s), 1000 (s), 901 (vs), 851 (s), 772 (vw), 737 (vw) cm^{-1}.

HRMS (EI): m/z for $C_{14}H_{18}O^+$ $[M]^+$: calcd.: 202.1352
found: 202.1342.

*5-Methylen-1,3,8-trimethyltricyclo[4.3.1.0^{3,7}]dec-8-en-2-one (**556**)*

$C_{14}H_{18}O$ M_r = 202.29 g·mol^{-1}.

TLC R_f = 0.49 (hexanes : EtOAc = 9 : 1).

^{1}H NMR (300 MHz, $CDCl_3$): δ = 5.58 – 5.48 (m, 1H, C9-H), 4.97 – 4.89 (m, 1H, C13-H_A), 4.74 – 4.67 (m, 1H, C13-H_B), 2.75 (dd, $^3J_{C6\text{-}H,C10\text{-}HA}$ = 10.3 Hz, $^3J_{C6\text{-}H,C7\text{-}H}$ = 4.7 Hz, 1H, C6-H), 2.52 (dd, $^3J_{C7\text{-}H,C6\text{-}H}$ = 4.7 Hz, $^4J_{C7\text{-}H,C4\text{-}H}$ = 2.2 Hz, 1H, C7-H), 2.42 – 2.33 (m, 1H, C4-H_A), 2.18 (ddd, $^2J_{C4\text{-}HB,C4\text{-}HA}$ = 17.4 Hz, $^4J_{C4\text{-}HB,C10\text{-}HA}$ = 2.6 Hz, $^4J_{C4\text{-}HB,C10\text{-}HB}$ = 2.6 Hz, 1H, C4-H_B), 1.84 (d, $^4J_{C14\text{-}H,C9\text{-}H}$ = 1.7 Hz, 3H, C14-H), 1.71 (dd, $^2J_{C10\text{-}HA,C10\text{-}HB}$ = 12.8 Hz, $^3J_{C10\text{-}HA,C6\text{-}H}$ = 10.3 Hz, 1H, C10-H_A), 1.28 (d, $^2J_{C10\text{-}HB,C10\text{-}HA}$ = 12.8 Hz, 1H, C10-H_B), 1.13 (s, 3H, C11-H), 1.09 (s, 3H, C12-H) ppm.

^{13}C NMR (75 MHz, $CDCl_3$): δ = 217.7 (C2), 154.8 (C5), 141.6 (C8), 127.4 (C9), 106.3 (C13), 55.3 (C7), 51.7 (C3), 48.3 (C1), 44.1 (C6), 42.7 (C10), 42.0 (C4), 21.9 (C14), 20.4 (C12), 17.8 (C11) ppm.

IR (ATR): $\tilde{\nu}$ = 3070 (vw), 3028 (vw), 2963 (w), 2926 (w), 2865 (vw), 1716 (vs), 1679 (vw), 1657 (w), 1440 (w), 1376 (w), 1334 (vw), 1297 (vw), 1262 (vw), 1221 (vw), 1184 (vw), 1158 (vw), 1119 (w), 1085 (vw), 1048 (vw), 1020 (w), 999 (vw), 971 (w), 922 (vw), 879 (m), 839 (w), 810 (w), 779 (w), 755 (vw), 708 (vw), 669 (vw) cm^{-1}.

HRMS (EI): m/z for $C_{14}H_{18}O^+$ $[M]^+$: calcd.: 202.1352

found: 202.1353.

*9-Methylen-1,3,5-trimethyltricyclo[4.4.0.0^{3,8}]dec-4-en-2-one (**558**)*

$C_{14}H_{18}O$ M_r = 202.29 g·mol^{-1}.

TLC R_f = 0.43 (hexanes : EtOAc = 9 : 1).

mp 65 – 67 °C.

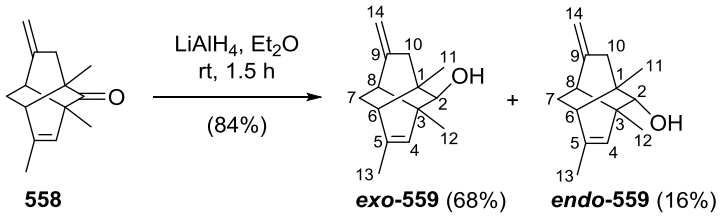
^{1}H NMR (600 MHz, $CDCl_3$): δ = 5.17 (dq, $^4J_{C4\text{-}H,C13\text{-}H}$ =1.8 Hz, $^4J_{C4\text{-}H,C6\text{-}H}$ = 1.6 Hz, 1H, C4-H), 4.77 – 4.73 (m, 1H, C14-H_A), 4.60 – 4.57 (m, 1H, C14-H_B), 2.38 (ddd, $^2J_{C10\text{-}H_A,C10\text{-}H_B}$ = 15.4 Hz, $^3J_{C10\text{-}H_A,C14\text{-}H_A}$ = 2.8 Hz, $^3J_{C10\text{-}H_A,C14\text{-}H_B}$ = 2.8 Hz, 1H, C10-H_A), 2.34 (ddd, $^3J_{C6\text{-}H,C7\text{-}H_A}$ = 5.4 Hz, $^4J_{C6\text{-}H,C8\text{-}H}$ = 1.6 Hz, $^4J_{C6\text{-}H,C4\text{-}H}$ = 1.6 Hz, 1H, C6-H), 2.11 (dd, $^3J_{C8\text{-}H,C7\text{-}H_B}$ = 6.3 Hz, $^4J_{C8\text{-}H,C6\text{-}H}$ = 1.6 Hz, 1H, C8-H), 2.00 – 1.94 (m, 2H, C7-H_A, C10-H_B), 1.83 (d, $^4J_{C13\text{-}H,C4\text{-}H}$ = 1.8 Hz, 3H, C13-H), 1.36 (dd, $^2J_{C7\text{-}H_B,C7\text{-}H_A}$ = 11.7 Hz, $^3J_{C7\text{-}H_B,C8\text{-}H}$ = 6.3 Hz, 1H, C7-H_B), 1.17 (s, 3H, C12-H), 1.00 (s, 3H, C11-H) ppm.

^{13}C NMR (150 MHz, $CDCl_3$): δ = 212.0 (C2), 151.3 (C5), 145.9 (C9), 122.3 (C4), 108.0 (C14), 54.1 (C3), 47.6 (C6), 45.4 (C8), 41.9 (C1), 40.8 (C10), 32.7 (C7), 20.6 (C13), 18.8 (C11), 14.3 (C12) ppm.

IR (ATR): $\tilde{\nu}$ = 3072 (vw), 3026 (vw), 2957 (w), 2926 (w), 2868 (vw), 1724 (vs), 1655 (vw), 1469 (vw), 1445 (w), 1403 (vw), 1373 (w), 1342 (vw), 1299 (vw), 1262 (vw), 1225 (vw), 1198 (vw), 1172 (vw), 1153 (vw), 1136 (vw), 1107 (vw), 1045 (w), 1033 (w), 988 (vw), 964 (w), 944 (vw), 923 (w), 883 (m), 859 (vw), 847 (vw), 833 (w), 797 (vw), 765 (w), 756 (w), 668 (vw) cm^{-1}.

HRMS (EI): m/z for $C_{14}H_{18}O^+$ $[M]^+$: calcd.: 202.1352
found: 202.1345.

Reduction of Twistenone 558



To a solution of ketone **558** (218 mg, 1.08 mmol, 1.00 eq.) in Et_2O (5.00 mL) at room temperature was added $LiAlH_4$ (50.0 mg, 1.32 mmol, 1.22 eq.). The resulting mixture was stirred at room temperature for 1.5 h and was then quenched by careful addition of saturated aqueous Rochelle salt. The mixture was extracted with Et_2O (3 x 20 mL) and the combined organic layer was washed with H_2O (40 mL), dried (Na_2SO_4) and concentrated *in vacuo*. Purification of the residue by flash column chromatography

(2 x 16 cm, silica, *n*-pentane : Et_2O = 97 : 3, 8 mL) afforded *exo*-alcohol ***exo*-559** (149 mg, 68%, #25─43) as a colorless oil and *endo*-alcohol ***endo*-559** (35 mg, 16%, #68─94) as a colorless oil.

*exo-9-Methylen-1,3,5-trimethyltricyclo[4.4.0.0^{3,8}]dec-4-en-2-ol (**exo-559**)*

$C_{14}H_{20}O$ M_r = 204.31 g·mol^{-1}.

TLC R_f = 0.24 (*n*-pentane : Et_2O = 95 : 5).

^{1}H NMR (400 MHz, DMSO-d_6): δ = 5.43 (dq, $^4J_{C4\text{-}H,C6\text{-}H}$ = 1.7 Hz, $^4J_{C4\text{-}H,C13\text{-}H}$ = 1.7 Hz, 1H, C4-H), 4.59 (ddd, $^2J_{C14\text{-}H_A,C14\text{-}H_B}$ = 2.6 Hz, $^4J_{C14\text{-}H_A,C10\text{-}H_B}$ = 2.6 Hz, $^4J_{C14\text{-}H_A,C10\text{-}H_A}$ = 1.1 Hz, 1H, C14-H_A), 4.40 (ddd, $^2J_{C14\text{-}H_B,C14\text{-}H_A}$ = 2.6 Hz, $^4J_{C14\text{-}H_B,C10\text{-}H_B}$ = 2.6 Hz, $^4J_{C14\text{-}H_B,C10\text{-}H_A}$ = 1.1 Hz, 1H, C14-H_B), 4.36 (dd, $^3J_{OH,C2\text{-}H}$ = 4.8 Hz, *J* = 1.6 Hz, 1H, OH), 2.66 (d, $^3J_{C2\text{-}H,OH}$ = 4.8 Hz, 1H, C2-H), 2.09 (ddd, $^2J_{C10\text{-}H_A,C10\text{-}H_B}$ = 14.9 Hz, $^4J_{C10\text{-}H_A,C14\text{-}H_A}$ = 1.1 Hz, $^4J_{C10\text{-}H_A,C14\text{-}H_B}$ = 1.1 Hz, 1H, C10-H_A), 1.97 (ddd, $^2J_{C10\text{-}H_B,C10\text{-}H_A}$ = 14.9 Hz, $^4J_{C10\text{-}H_B,C14\text{-}H_A}$ = 2.6 Hz, $^4J_{C10\text{-}H_B,C14\text{-}H_B}$ = 2.6 Hz, 1H, C10-H_B), 1.91 (ddd, $^3J_{C6\text{-}H,C7\text{-}H_A}$ = 5.4 Hz, $^4J_{C6\text{-}H,C4\text{-}H}$ = 1.7 Hz, $^4J_{C6\text{-}H,C8\text{-}H}$ = 1.3 Hz, 1H, C6-H), 1.76 (d, $^4J_{C13\text{-}H,C4\text{-}H}$ = 1.7 Hz, 3H, C13-H), 1.72 (dd, $^2J_{C7\text{-}H_A,C7\text{-}H_B}$ = 10.9 Hz, $^3J_{C7\text{-}H_A,C6\text{-}H}$ = 5.4 Hz, 1H, C7-H_A), 1.59 (dd, $^3J_{C8\text{-}H,C7\text{-}H_B}$ = 6.1 Hz, $^4J_{C8\text{-}H,C6\text{-}H}$ = 1.3 Hz, 1H, C8-H), 1.08 (dd, $^2J_{C7\text{-}H_B,C7\text{-}H_A}$ = 10.9 Hz, $^3J_{C7\text{-}H_B,C8\text{-}H}$ = 6.1 Hz, 1H, C7-H_B), 0.95 (s, 3H, C12-H), 0.81 (s, 3H, C11-H) ppm.

^{13}C NMR (100 MHz, DMSO-d_6): δ = 150.8 (C9), 142.5 (C5), 130.8 (C4), 103.1 (C14), 83.7 (C2), 46.3 (C6), 44.0 (C3), 42.3 (C8), 36.7 (C7), 34.4 (C10), 31.9 (C1), 24.3 (C11), 20.4 (C13), 18.0 (C12) ppm.

IR (ATR): $\tilde{\nu}$ = 3493 (br vw), 3027 (vw), 2946 (vs), 2922 (vs), 2865 (m), 1658 (vw), 1479 (vw), 1444 (m), 1381 (w), 1330 (w), 1308 (vw), 1299 (vw), 1275 (w), 1216 (vw), 1196 (vw), 1156 (w), 1118 (w), 1048 (w), 1008 (vs), 978 (w), 946 (w), 910 (w), 898 (w), 885 (s), 846 (m), 810 (s), 790 (w), 668 (w) cm^{-1}.

HRMS (EI): m/z for $C_{14}H_{20}O^+$ $[M]^+$: calcd.: 204.1509
found: 204.1501.

*endo-9-Methylen-1,3,5-trimethyltricyclo[4.4.0.0^{3,8}]dec-4-en-2-ol (**endo-559**)*

$C_{14}H_{20}O$ M_r = 204.31 g·mol^{-1}.

TLC R_f = 0.18 (*n*-pentane : Et_2O = 95 : 5).

^{1}H NMR (400 MHz, DMSO-d_6): δ = 5.11 (dq, $^4J_{C4\text{-}H,C6\text{-}H}$ = 1.7 Hz, $^4J_{C4\text{-}H,C13\text{-}H}$ = 1.7 Hz, 1H, C4-H), 4.71 (ddd, $^2J_{C14\text{-}H_A,C14\text{-}H_B}$ = 2.3 Hz, $^4J_{C14\text{-}H_A,C10\text{-}H_A}$ = 2.3 Hz, $^4J_{C14\text{-}H_A,C10\text{-}H_B}$ = 1.1 Hz, 1H, C14-H_A), 4.59 (ddd, $^2J_{C14\text{-}H_B,C14\text{-}H_A}$ = 2.3 Hz, $^4J_{C14\text{-}H_B,C10\text{-}H_A}$ = 2.3 Hz, $^4J_{C14\text{-}H_B,C10\text{-}H_B}$ = 1.1 Hz, 1H, C14-H_B), 3.36 (dd, $^3J_{OH,C2\text{-}H}$ = 8.7 Hz, *J* = 0.9 Hz, 1H, OH), 2.91 (d, $^3J_{C2\text{-}H,OH}$ = 8.7 Hz, 1H, C2-H), 2.28 (ddd, $^2J_{C10\text{-}H_A,C10\text{-}H_B}$ = 15.0 Hz, $^4J_{C10\text{-}H_A,C14\text{-}H_A}$ = 2.3 Hz, $^4J_{C10\text{-}H_A,C14\text{-}H_B}$ = 2.3 Hz, 1H, C10-H_A), 1.88 (dd, $^3J_{C6\text{-}H,C7\text{-}H_A}$ = 5.2 Hz, $^4J_{C6\text{-}H,C4\text{-}H}$ = 1.7 Hz, $^4J_{C6\text{-}H,C8\text{-}H}$ = 1.1 Hz, 1H,

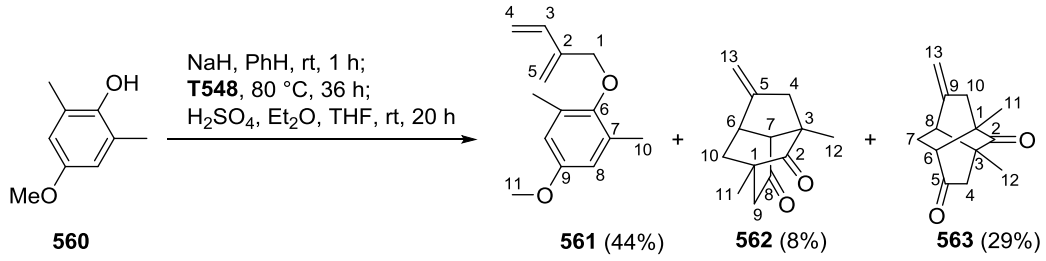
C6-H), 1.83 (d, $^4J_{C13\text{-}H,C4\text{-}H}$ = 1.7 Hz, 3H, C13-H), 1.76 (ddd, $^2J_{C10\text{-}H_B,C10\text{-}H_A}$ = 15.0 Hz, $^4J_{C10\text{-}H_B,C14\text{-}H_A}$ = 1.1 Hz, $^4J_{C10\text{-}H_B,C14\text{-}H_B}$ = 1.1 Hz, 1H, C10-H_B), 1.70 (dd, $^3J_{C8\text{-}H,C7\text{-}H_B}$ = 6.2 Hz, $^4J_{C8\text{-}H,C6\text{-}H}$ = 1.1 Hz, 1H, C8-H), 1.61 (dd, $^2J_{C7\text{-}H_A,C7\text{-}H_B}$ = 11.0 Hz, $^3J_{C7\text{-}H_A,C6\text{-}H}$ = 5.3 Hz, 1H, C7-H_A), 1.09 (s, 3H, C12-H), 0.99 (dd, $^2J_{C7\text{-}H_B,C7\text{-}H_A}$ = 11.0 Hz, $^3J_{C7\text{-}H_B,C8\text{-}H}$ = 6.2 Hz, 1H, C7-H_B), 0.77 (s, 3H, C11-H) ppm.

^{13}C NMR (100 MHz, DMSO-d_6): δ = 149.0 (C5), 147.3 (C9), 124.2 (C4), 106.1 (C14), 81.9 (C2), 46.2 (C6), 44.5 (C3), 43.6 (C8), 42.2 (C10), 38.4 (C1), 35.6 (C7), 21.5 (C11), 20.5 (C13), 19.2 (C12) ppm.

IR (ATR): $\tilde{\nu}$ = 3555 (vw), 3480 (br vw), 3068 (vw), 3020 (vw), 2952 (s), 2922 (s), 2867 (w), 1652 (w), 1453 (m), 1436 (m), 1416 (w), 1373 (w), 1331 (vw), 1298 (vw), 1278 (w), 1260 (w), 1239 (vw), 1195 (vw), 1150 (m), 1110 (m), 1084 (w), 1064 (vs), 1011 (vw), 981 (vw), 950 (vw), 877 (vs), 835 (w), 816 (m), 783 (w), 731 (vw), 668 (vw), 635 (w) cm^{-1}.

HRMS (EI): m/z for $C_{14}H_{20}O^+$ $[M]^+$: calcd.: 204.1509
found: 204.1509.

Allylation/Claisen/Diels-Alder Cascade of Mesitol (560)



560 **561** (44%) **562** (8%) **563** (29%)

To a suspension of NaH (1.94 g, 48.5 mmol, 1.26 eq.) in benzene (36.5 mL) was added slowly a solution of methoxyphenol **560** (7.03 g, 46.2 mmol, 1.20 eq.) in benzene (91.2 mL). After complete addition the reaction mixture was stirred at room temperature for 15 min. Then, freshly distilled bromodiene **551** (5.66 g, 38.5 mmol, 1.00 eq.) was added and the resulting mixture was stirred at 80 °C for 36 h. The mixture was allowed to cool to room temperature and H_2O was added (285 mL). The mixture was extracted with *n*-pentane (5 x 115 mL) and the combined organic layers were washed with 10 wt-% aqueous NaOH (170 mL), Claisen lye (115 mL), H_2O (170 mL), dried (Na_2SO_4) and concentrated *in vacuo*. The crude reaction mixture was dissolved in Et_2O (142 mL) and THF (71 mL) and was treated with 2 N H_2SO_4 (43 mL). The resulting mixture was stirred at room temperature for 20 h and was then neutralized with 1 N NaOH (43 mL). The organic layer was separated, dried (Na_2SO_4) and concentrated *in vacuo*. Purification of the residue by flash column chromatography (5 x 25 cm, silica, *n*-pentane : Et_2O = 4 : 1, 100 mL) afforded ether **561** (3.71 g, 44%, #6-10) as a colorless oil, isotwistadione **562** (0.63 g, 8%, #18-22) as a colorless oil and twistadione **563** (2.31 g, 29%,

#26–45) as a colorless solid. Recrystallization of twistadione **563** from hexanes afforded crystals suitable for single crystal X-ray diffraction.

*2,6-Dimethyl-4-methoxyphenyl-(2-methylen-3-butenyl)ether (**561**)*

$C_{14}H_{18}O_2$ M_r = 218.30 g·mol^{-1}.

TLC R_f = 0.64 (hexanes : EtOAc = 9 : 1).

^{1}H NMR (300 MHz, $CDCl_3$): δ = 6.60 – 6.56 (m, 2H, C8-H), 6.53 – 6.42 (m, 1H, C3-H), 5.56 – 5.52 (m, 1H, C5-H_A), 5.33 – 5.25 (m, 2H, C4-H_A, C5-H_B), 5.17 – 5.11 (m, 1H, C4-H_B), 4.44 – 4.42 (m, 2H, C1-H), 3.76 (s, 3H, C11-H), 2.30 – 2.27 (m, 6H, C10-H) ppm.

^{13}C NMR (75 MHz, $CDCl_3$): δ = 155.5 (C9), 150.0 (C6), 142.5 (C2), 136.8 (C3), 132.0 (C7), 116.8 (C5), 113.9 (C4), 113.8 (C8), 71.6 (C1), 55.5 (C11), 16.7 (C10) ppm.

IR (ATR): $\tilde{\nu}$ = 3089 (vw), 3044 (vw), 2997 (vw), 2939 (vw), 2920 (vw), 2859 (vw), 2838 (vw), 1817 (vw), 1642 (vw), 1597 (m), 1541 (vw), 1484 (m), 1466 (m), 1440 (w), 1393 (vw), 1375 (vw), 1325 (w), 1278 (vw), 1236 (w), 1203 (vs), 1150 (m), 1064 (s), 1015 (m), 994 (m), 956 (vw), 940 (vw), 903 (s), 856 (m), 836 (w), 771 (w), 732 (vw), 668 (vw), 611 (vw) cm^{-1}.

HRMS (EI): m/z for $C_{14}H_{18}O_2^+$ $[M]^+$: calcd.: 218.1301
found: 218.1299.

*1,3-Dimethyl-5-methylenetriycyclo[4.3.1.0^{3,7}]decan-2,8-dione (**562**)*

$C_{13}H_{16}O_2$ M_r = 204.27 g·mol^{-1}.

TLC R_f = 0.19 (hexanes : EtOAc = 9 : 1).

^{1}H NMR (600 MHz, $CDCl_3$): δ = 5.02 – 5.00 (m, 1H, C13-H_A), 4.84 – 4.81 (m, 1H, C13-H_B), 3.14 – 3.08 (m, 1H, C6-H), 2.60 (d, $^3J_{C7\text{-}H,C6\text{-}H}$ = 5.1 Hz, 1H, C7-H), 2.59 – 2.54 (m, 1H, C4-H_A), 2.26 – 2.21 (m, 3H, C4-H_B, C9-H), 2.10 (dd, $^2J_{C10\text{-}HA,C10\text{-}HB}$ = 13.7 Hz, $^3J_{C10\text{-}HA,C6\text{-}H}$ = 9.5 Hz, 1H, C10-H_A), 1.49 – 1.46 (m, 1H, C10-H_B), 1.17 (s, 3H, C12-H), 1.06 (s, 3H, C11-H) ppm.

^{13}C NMR (150 MHz, $CDCl_3$): δ = 217.2 (C2), 211.2 (C8), 153.1 (C5), 108.0 (C13), 62.2 (C7), 55.4 (C3), 47.9 (C9), 44.8 (C1), 43.8 (C6), 43.2 (C4), 40.2 (C10), 19.4 (C12), 19.3 (C11) ppm.

IR (ATR): $\tilde{\nu}$ = 3430 (vw), 3075 (vw), 2966 (vw), 2931 (w), 2901 (vw), 2870 (vw), 1712 (vs), 1660 (vw), 1456 (w), 1404 (vw), 1379 (vw), 1298 (vw), 1229 (m), 1178 (vw), 1163 (vw), 1140 (vw), 1086 (vw), 1040 (vw), 1018 (w), 982 (w), 917 (vw), 885 (w), 799 (vw) cm^{-1}.

HRMS (EI): m/z for $C_{13}H_{16}O_2^+$ $[M]^+$: calcd.: 204.1145
found: 204.1137.

*1,3-Dimethyl-9-methylenetriycyclo[4.4.0.0^{3,8}]decan-2,5-dione (**563**)*

$C_{13}H_{16}O_2$ M_r = 204.27 g·mol^{-1}.

TLC R_f = 0.13 (hexanes : EtOAc = 9 : 1).

mp 82 – 85 °C.

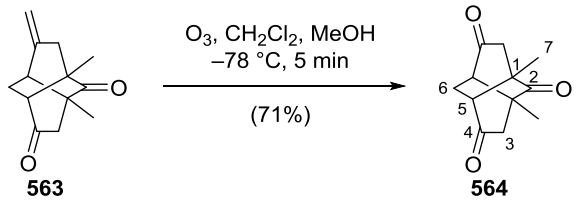
^{1}H NMR (600 MHz, $CDCl_3$): δ = 4.88 (dddd, $^2J_{C13\text{-}H_A,C13\text{-}H_B}$ = 2.5 Hz, $^4J_{C13\text{-}H_A,C10\text{-}H_A}$ = 0.9 Hz, $^4J_{C13\text{-}H_A,C10\text{-}H_B}$ = 0.9 Hz, $^4J_{C13\text{-}H_A,C8\text{-}H}$ = 0.5 Hz, 1H, C13-H_A), 4.76 (ddd, $^2J_{C13\text{-}H_B,C13\text{-}Ha}$ = 2.5 Hz, $^4J_{C13\text{-}H_B,C10\text{-}H_A}$ = 1.2 Hz, $^4J_{C13\text{-}H_B,C10\text{-}H_B}$ = 1.2 Hz, 1H, C13-H_B), 2.73 (d, $^2J_{C4\text{-}H_A,C4\text{-}H_B}$ = 17.9 Hz, 1H, C4-H_A), 2.72 – 2.68 (m, 1H, C10-H_A), 2.56 – 2.53 (m, 1H, C8-H), 2.53 – 2.50 (m, 1H, C6-H), 2.20 – 2.11 (m, 3H, C7-H, C10-H_B), 2.04 (d, $^2J_{C4\text{-}H_B,C4\text{-}H_A}$ = 17.9 Hz, 1H, C4-H_B), 1.08 (s, 3H, C12-H), 1.06 (s, 3H, C11-H) ppm.

^{13}C NMR (150 MHz, $CDCl_3$): δ = 217.1 (C2), 208.7 (C5), 144.1 (C9), 109.7 (C13), 54.4 (C6), 50.0 (C3), 46.8 (C8), 46.8 (C1), 45.1 (C4), 39.8 (C10), 25.3 (C7), 17.1 (C11), 15.6 (C12) ppm.

IR (ATR): $\tilde{\nu}$ = 2966 (w), 2929 (vw), 2900 (vw), 2871 (vw), 1729 (vs), 1656 (vw), 1454 (vw), 1292 (vw), 1221 (w), 1192 (vw), 1172 (vw), 1137 (vw), 1126 (vw), 1088 (vw), 1027 (w), 990 (vw), 972 (vw), 955 (vw), 889 (vw), 844 (vw) cm^{-1}.

HRMS (EI): m/z for $C_{13}H_{16}O_2^+$ $[M]^+$: calcd.: 204.1145
found: 204.1154.

1,3-Dimethyltricyclo[4.4.0.0^{3,8}]decan-2,5,9-trione (564)



Through a solution of diketone **563** (239 mg, 1.17 mmol, 1.00 eq.) in CH_2Cl_2 (5.00 mL) and MeOH (5.00 mL) at −78 °C was bubbled ozone until a blue color persisted in the reaction mixture. Excess ozone was removed by bubbling argon through the reaction mixture and simultaneously warming to room temperature. The reaction mixture was transferred to another flask and was diluted with 20 mL MeOH. Pd on activated charcoal (10 wt-%, 50 mg) was added and the reaction mixture was treated with hydrogen by means of a balloon for 2 h at room temperature. The catalyst was filtered off over celite and to the filtrate was added some water. The aqueous layer was extracted with CH_2Cl_2 (3 x 20 mL) and the combined organic layer was dried (Na_2SO_4) and concentrated *in vacuo*. Purification of the residue by flash column chromatography (3 x 14 cm, silica, hexanes : EtOAc = 3 : 1, 20 mL, #40–78) afforded trione **564** (171 mg, 71%) as a colorless solid. Recrystallization from *n*-pentane afforded crystals which were suitable for single crystal X-ray diffraction.

$C_{12}H_{14}O_3$ M_r = 206.24 g·mol^{-1}.

TLC R_f = 0.24 (hexanes : EtOAc = 3 : 1).

mp 178 – 180 °C.

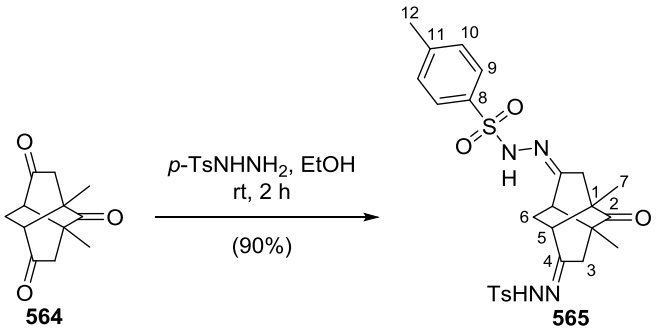
^{1}H NMR (600 MHz, $CDCl_3$): δ = 2.87 (d, $^2J_{C3\text{-}HA,C3\text{-}HB}$ = 18.0 Hz, 2H, C3-H_A), 2.71 (dd, $^3J_{C5\text{-}H,C6\text{-}HA}$ = 3.6 Hz, $^3J_{C5\text{-}H,C6\text{-}HB}$ = 2.7 Hz, 2H, C5-H), 2.36 – 2.33 (m, 2H, C6-H), 2.16 (d, $^2J_{C3\text{-}HB,C3\text{-}HA}$ = 18.0 Hz, 2H, C3-H_B), 1.16 (s, 6H, C7-H) ppm.

^{13}C NMR (150 MHz, $CDCl_3$): δ = 213.4 (C2), 206.2 (C4), 53.3 (C5), 47.5 (C1), 45.7 (C3), 23.5 (C6), 16.7 (C7) ppm.

IR (ATR): $\tilde{\nu}$ = 3444 (vw), 2966 (w), 2948 (vw), 2931 (vw), 2873 (vw), 1742 (m), 1725 (vs), 1670 (w), 1597 (vw), 1470 (vw), 1451 (w), 1410 (w), 1377 (w), 1318 (vw), 1291 (vw), 1218 (m), 1194 (w), 1170 (vw), 1129 (w), 1080 (vw), 1019 (m), 980 (vw), 944 (vw), 913 (vw), 884 (vw), 836 (vw), 818 (vw), 760 (w), 734 (vw), 668 (vw), 632 (vw) cm^{-1}.

HRMS (EI): m/z for $C_{12}H_{14}O_3^+$ $[M]^+$: calcd.: 206.0938
found: 206.0935.

1,3-Dimethyltricyclo[4.4.0.0^{3,8}]decan-2-one-5,9-bistosylhydrazone (565)



To a solution of tosylhydrazide (451 mg, 2.42 mmol, 2.00 eq.) in EtOH (6.00 mL) was added a solution of triketone **564** (250 mg, 1.21 mmol, 1.00 eq.) in EtOH (2.50 mL). The resulting mixture was stirred at room temperature for 15 min and was then allowed to stand at room temperature for an additional 2 h. The precipitated white solid was filtered off, washed with cold EtOH (10 mL) and dried *in vacuo* to afford bistosylhydrazone **565** (592 mg, 90%) as a colorless solid.

$C_{26}H_{30}N_4O_5S_2$ M_r = 542.68 g·mol^{-1}.

TLC R_f = 0.12 (hexanes : EtOAc = 3 : 1).

mp 217 – 221 °C.

^{1}H NMR (400 MHz, DMSO-d_6): δ = 10.15 (s, 2H, N-H), 7.69 – 7.65 (m, 4H, C9-H), 7.39 – 7.34 (m, 4H, C10-H), 2.58 (d, $^2J_{C3\text{-}HA,C3\text{-}HB}$ = 17.6 Hz, 2H, C3-H_A), 2.44 (dd, $^3J_{C5\text{-}H,C6\text{-}HA}$ = 3.5 Hz, $^3J_{C5\text{-}H,C6\text{-}HB}$ = 2.7 Hz, 2H, C5-H), 2.37 (s, 6H, C12-H), 2.31 (d,

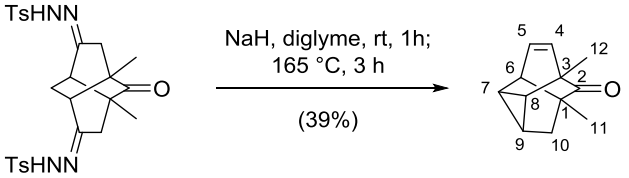
$^{2}J_{C3\text{-}HB,C3\text{-}HA}$ = 17.6 Hz, 2H, C3-H_B), 1.92 – 1.87 (m, 2H, C6-H), 0.76 (s, 6H, C7-H) ppm.

^{13}C NMR (100 MHz, DMSO-d_6): δ = 216.8 (C2), 157.6 (C4), 143.1 (C11), 136.1 (C8), 129.3 (C10), 127.2 (C9), 46.6 (C1), 45.7 (C5), 34.7 (C3), 25.7 (C6), 21.0 (C12), 15.5 (C7) ppm.

IR (ATR): $\tilde{\nu}$ = 3215 (vw), 2957 (vw), 1740 (w), 1596 (vw), 1447 (vw), 1402 (w), 1337 (m), 1291 (vw), 1237 (vw), 1181 (vw), 1167 (vs), 1120 (vw), 1091 (w), 1044 (w), 1022 (w), 970 (vw), 922 (w), 899 (w), 847 (vw), 811 (w), 782 (w), 706 (w), 672 (vs) cm^{-1}.

HRMS (EI): m/z for $C_{26}H_{30}N_4O_5S_2^+$ $[M]^+$: calcd.: 542.1652
found: 542.1648.

1,3-Dimethyltetracyclo[4.4.0.0^{3,8}.0^{7,9}]dec-4-en-2-one (567)



565 **567**

To a solution of bistosylhydrazone **565** (200 mg, 0.368 mmol, 1.00 eq.) in diglyme (6.00 mL) at room temperature was added NaH (30.0 mg, 1.25 mmol, 3.40 eq.) and the resulting mixture was stirred at room temperature for 15 min. The reaction mixture was diluted with diglyme (6.00 mL) and was subsequently heated to 165 °C for 3 h. The reaction mixture was allowed to cool to room temperature and was quenched by addition of H_2O (10 mL). The mixture was extracted with Et_2O (3 x 15 mL) and the combined organic layer was washed with H_2O (5 x 15 mL), brine (2 x 10 mL), dried (Na_2SO_4) and concentrated *in vacuo*. Purification of the residue by flash column chromatography (2 x 14 cm, silica, *n*-pentane : Et_2O = 95 : 5, 8 mL, #14–22) afforded tetracyclic ketone **567** (25 mg, 39%) as a colorless solid. Recrystallization from *n*-pentane afforded crystals suitable for single crystal X-ray diffraction.

$C_{12}H_{14}O$ M_r = 174.24 g·mol^{-1}.

TLC R_f = 0.17 (hexanes : EtOAc = 95 : 5).

mp 42 – 44 °C.

^{1}H NMR (400 MHz, $CDCl_3$): δ = 6.39 (dd, $^{3}J_{C5\text{-}H,C4\text{-}H}$ = 7.4 Hz, $^{3}J_{C5\text{-}H,C6\text{-}H}$ = 6.0 Hz, 1H, C5-H), 5.77 (dd, $^{3}J_{C4\text{-}H,C5\text{-}H}$ = 7.4 Hz, $^{4}J_{C4\text{-}H,C6\text{-}H}$ = 1.5 Hz, 1H, C4-H), 2.96 (dddd, $^{3}J_{C6\text{-}H,C5\text{-}H}$ = 6.0 Hz, $^{3}J_{C6\text{-}H,C7\text{-}H}$ = 4.2 Hz, $^{4}J_{C6\text{-}H,C4\text{-}H}$ = 1.5 Hz, $^{4}J_{C6\text{-}H,C8\text{-}H}$ = 1.5 Hz, 1H, C6-H), 2.18 (ddd, $^{2}J_{C10\text{-}Hanti,C10\text{-}Hsyn}$ = 12.7 Hz, $^{3}J_{C10\text{-}Hanti,C9\text{-}H}$ = 2.6 Hz, $^{4}J_{C10\text{-}Hanti,C8\text{-}H}$ = 1.5 Hz, 1H, C10-H_{anti}), 2.08 (dd, $^{2}J_{C10\text{-}Hsyn,C10\text{-}Hanti}$ = 12.7 Hz, $^{2}J_{C10\text{-}Hsyn,C9\text{-}H}$ = 1.1 Hz, 1H, C10-H_{syn}), 1.84 (ddd, $^{3}J_{C7\text{-}H,C8\text{-}H}$ = 8.3 Hz,

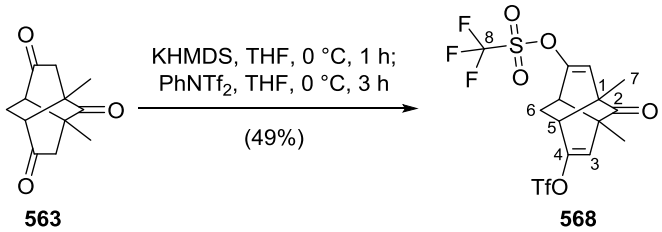
$^3J_{C7\text{-}H,C9\text{-}H}$ = 5.5 Hz, $^3J_{C7\text{-}H,C6\text{-}H}$ = 4.2 Hz, 1H, C7-H), 1.48 (dddd, $^3J_{C9\text{-}H,C8\text{-}H}$ = 6.6 Hz, $^3J_{C9\text{-}H,C7\text{-}H}$ = 5.5 Hz, $^3J_{C9\text{-}H,C10\text{-}Hanti}$ = 2.6 Hz, $^3J_{C9\text{-}H,C10\text{-}Hsyn}$ = 1.1 Hz, 1H, C9-H), 1.40 (s, 3H, C12-H), 1.17 (dddd, $^3J_{C8\text{-}H,C7\text{-}H}$ = 8.3 Hz, $^3J_{C8\text{-}H,C9\text{-}H}$ = 6.6 Hz, $^4J_{C8\text{-}H,C10\text{-}Hanti}$ = 1.5 Hz, $^4J_{C8\text{-}H,C6\text{-}H}$ = 1.5 Hz, 1H, C8-H), 1.00 (s, 3H, C11-H) ppm.

^{13}C NMR (150 MHz, $CDCl_3$): δ = 212.3 (C2), 135.5 (C5), 134.8 (C4), 50.1 (C3), 48.6 (C6), 47.2 (C1), 44.8 (C10), 28.2 (C8), 27.9 (C7), 22.3 (C9), 17.9 (C11), 17.4 (C12) ppm.

IR (ATR): $\tilde{\nu}$ = 3043 (vw), 2961 (w), 2929 (w), 2863 (vw), 1724 (vs), 1456 (vw), 1376 (vw), 1333 (vw), 1268 (vw), 1213 (vw), 1159 (vw), 1099 (vw), 1016 (vw), 1002 (w), 896 (vw), 850 (vw), 808 (vw), 766 (vw), 692 (w) cm^{-1}.

HRMS (EI): m/z for $C_{12}H_{14}O^+$ $[M]^+$: calcd.: 174.1039
found: 174.1047.

1,3-Dimethyl-2-oxotricyclo[4.4.0.0^{3,8}]deca-4,9-diene-5,9-diyl bistriflate (568)



563 **568**

To a solution of triketone **563** (49.9 mg, 0.242 mmol, 1.00 eq.) in THF (1.65 mL) at 0 °C was added a solution of KHMDS in toluene (0.5 M, 1.26 mL, 0.629 mmol, 2.60 eq.) and the resulting mixture was stirred at 0 °C for 1 h. Then, a solution of $PhNTf_2$ (225 mg, 0.629 mmol, 2.60 eq.) in THF (0.600 mL) was added dropwise and the reaction mixture was stirred for an additional 3 h at 0 °C, after which time the reaction was quenched by addition of saturated aqueous $NaHCO_3$ (6 mL). The mixture was allowed to warm to room temperature and was then extracted with Et_2O (2 x 12 mL). The combined organic layer was washed with saturated aqueous $NaHCO_3$ (6 mL), dried (K_2CO_3) and concentrated *in vacuo*. Purification of the residue by flash column chromatography (3 x 14 cm, silica, hexanes : Et_2O = 3 : 1, 20 mL, #4─7) afforded bistriflate **568** (56 mg, 49%) as a colorless oil.

$C_{14}H_{12}F_6O_7S_2$ M_r = 470.37 g·mol^{-1}.

TLC R_f = 0.72 (hexanes : EtOAc = 3 : 1).

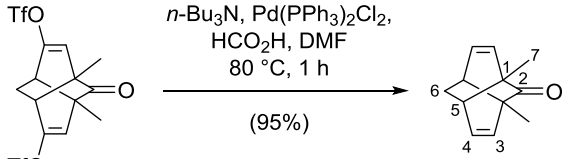
^{1}H NMR (600 MHz, $CDCl_3$): δ = 5.45 (d, $^3J_{C3\text{-}H,C5\text{-}H}$ = 2.6 Hz, 2H, C3-H), 2.66 (dt, $^3J_{C5\text{-}H,C6\text{-}H}$ = 3.8 Hz, $^3J_{C5\text{-}H,C3\text{-}H}$ = 2.6 Hz, 2H, C5-H), 2.11 (dd, $^3J_{C6\text{-}H,C5\text{-}H}$ = 3.7 Hz, $^2J_{C6\text{-}H_A,C6\text{-}H_B}$ = 2.7 Hz, 2H, C6-H), 1.55 (s, 6H, C7-H) ppm.

^{13}C NMR (150 MHz, $CDCl_3$): δ = 195.9 (C2), 156.5 (C4), 118.4 (q, $^1J_{C8,C8\text{-}F}$ = 325.2 Hz, C8), 117.6 (C3), 45.9 (C1), 42.3 (C6), 42.2 (C5), 16.8 (C7) ppm.

IR (ATR): $\tilde{\nu}$ = 2978 (vw), 1739 (m), 1630 (w), 1491 (vw), 1442 (m), 1422 (s), 1385 (vw), 1327 (vw), 1286 (vw), 1246 (m), 1205 (vs), 1128 (vs), 1068 (s), 1040 (s), 1010 (vw), 943 (m), 923 (vw), 884 (m), 869 (s), 835 (vs), 808 (w), 774 (vw), 743 (m), 693 (m) cm^{-1}.

HRMS (EI): m/z for $C_{14}H_{12}F_6O_7S_2^+$ $[M]^+$: calcd.: 469.9923
found: 469.9881.

1,3-Dimethyltricyclo[4.4.0.0^{3,8}]deca-4,9-dien-2-one (569)



568 **569**

To a mixture of bisenoltriflate **568** (114 mg, 0.242 mmol, 1.00 eq.), *n*-Bu_3N (0.346 mL, 269 mg, 1.45 mmol, 6.00 eq.) and $Pd(PPh_3)_2Cl_2$ (10.2 mg, 14.5 µmol, 0.060 eq.) in degassed DMF (2.00 mL) was added formic acid (36.5 µL, 44.6 mg, 0.968 mmol, 4.00 eq.) and the resulting mixture was stirred at 80 °C for 1 h. The mixture was allowed to cool to room temperature and H_2O (2 mL) was added. The mixture was extracted with Et_2O (3 x 5 mL) and the combined organic layer was dried (Na_2SO_4) and concentrated *in vacuo*. Purification of the residue by flash column chromatography (2 x 12 cm, silica, hexanes : Et_2O = 3 : 1, 8 mL, #10─13) afforded diene **569** (40 mg, 95%) as a colorless solid. Recrystallization from hexanes afforded crystals suitable for single crystal X-ray diffraction.

$C_{12}H_{14}O$ M_r = 174.24 g·mol^{-1}.

TLC R_f = 0.32 (hexanes : EtOAc = 9 : 1).

mp 76 – 78 °C.

^{1}H NMR (600 MHz, $CDCl_3$): δ = 6.60 (dd, $^3J_{C4\text{-}H,C3\text{-}H}$ = 7.7 Hz, $^3J_{C4\text{-}H,C5\text{-}H}$ = 6.1 Hz, 2H, C4-H), 5.51 (dd, $^3J_{C3\text{-}H,C4\text{-}H}$ = 7.7 Hz, $^4J_{C3\text{-}H,C5\text{-}H}$ = 1.5 Hz, 2H, C3-H), 2.31 – 2.27 (m, 2H, C5-H), 1.58 (dd, $^3J_{C6\text{-}H,C5\text{-}H}$ = 4.1 Hz, $^3J_{C6\text{-}H,C5\text{-}H}$ = 2.6 Hz, 2H, C6-H), 1.31 (s, 6H, C7-H) ppm.

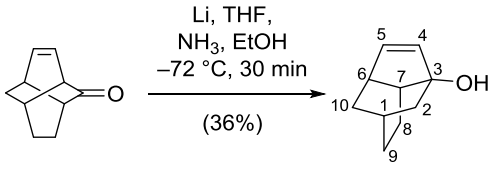
^{13}C NMR (150 MHz, $CDCl_3$): δ = 203.9 (C2), 140.6 (C4), 131.6 (C3), 46.5 (C1), 41.0 (C6), 38.2 (C5), 18.0 (C7) ppm.

IR (ATR): $\tilde{\nu}$ = 3402 (vw), 3044 (vw), 2961 (w), 2948 (w), 2941 (w), 2925 (m), 2867 (w), 2849 (w), 1707 (vs), 1669 (w), 1590 (vw), 1444 (m), 1375 (w), 1357 (w), 1348 (vw), 1287 (vw), 1231 (m), 1183 (w), 1096 (w), 1041 (m), 1011 (w), 978 (s), 949 (w), 929 (m), 877 (w), 836 (vw), 810 (s), 739 (vs), 734 (vs), 691 (s), 684 (s) cm^{-1}.

HRMS (EI): m/z for $C_{12}H_{14}O^+$ $[M]^+$: calcd.: 174.1039
found: 174.1054.

7.3 Synthesis of Twistanamines

3-Hydroxytricyclo[4.3.1.0^{3,7}]dec-4-ene (591)



470 **591**

A solution of ketone **470** (19.3 mg, 0.130 mmol, 1.00 eq.) in THF (1.00 mL) was added at ─72 °C to liquid ammonia (4.00 mL). Ethanol (0.422 mL) was added and then lithium (35.2 mg, 5.07 mmol, 39.0 eq.) was added in small pieces over the course of 1 h. The reaction mixture turned blue upon addition of lithium and turned colorless about 10 min after addition. After the last addition the mixture was stirred at ─72 °C for 30 min and was then allowed to warm slowly to room temperature thereby allowing the ammonia to evaporate. The mixture was diluted with H_2O (20 mL), acidified with 1 M HCl and extracted with Et_2O (3 x 25 mL). The combined organic layer was dried (Na_2SO_4) and concentrated *in vacuo*. Purification of the residue by flash column chromatography (2 x 15 cm, silica, *n*-pentane : Et_2O = 3 : 1, 8 mL, #26─35) afforded tertiary alcohol **591** (7 mg, 36%) as a colorless oil.

$C_{10}H_{14}O$ M_r = 150.22 g·mol^{-1}.

TLC R_f = 0.49 (hexanes : EtOAc = 3 : 1).

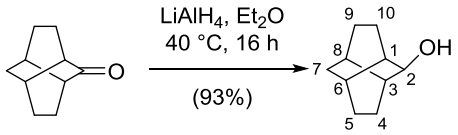
^{1}H NMR (400 MHz, $CDCl_3$): δ = 6.09 – 6.05 (m, 1H, C5-H), 5.96 – 5.93 (m, 1H, C4-H), 2.55 – 2.48 (m, 1H, C6-H), 2.04 – 1.95 (m, 2H, C2-H_A, C8-H_A), 1.95 – 1.87 (m, 2H, C1-H, C7-H), 1.74 – 1.59 (m, 1H, C8-H_B), 1.59 – 1.44 (m, 2H, C9-H), 1.43 – 1.36 (m, 1H, C2-H_B), 1.36 – 1.24 (m, 2H, C10-H) ppm.

^{13}C NMR (100 MHz, $CDCl_3$): δ = 142.1 (C4), 138.6 (C5), 80.5 (C3), 48.3 (C7), 40.2 (C6), 38.2 (C2), 29.0 (C1), 28.2 (C9), 27.7 (C10), 16.0 (C8) ppm.

IR (ATR): $\tilde{\nu}$ = 3378 (w), 3060 (vw), 2926 (vs), 2863 (m), 1733 (w), 1603 (vw), 1451 (vw), 1384 (vw), 1344 (w), 1285 (vw), 1188 (w), 1130 (w), 1108 (vw), 1081 (vw), 1050 (w), 1038 (w), 934 (vw), 880 (vw), 839 (vw), 813 (vw), 731 (w) cm^{-1}.

HRMS (EI): m/z for $C_{10}H_{14}O^+$ $[M]^+$: calcd.: 150.1039
found: 150.1044.

2-Hydroxytricyclo[4.4.0.0^{3,8}]decane (592)



253 **592**

To a solution of ketone **253** (200 mg, 1.33 mmol, 1.00 eq.) in Et_2O (25.0 mL) was added $LiAlH_4$ (23.9 mg, 2.66 mmol, 2.00 eq.). The resulting mixture was refluxed for 16 h and was then allowed to cool to room temperature. The reaction was quenched by dropwise addition of Rochelle salt and the resulting mixture was allowed to stir for 2 h. The organic layer was separated and the aqueous layer was extracted with Et_2O (3 x 50 mL). The combined organic layer was washed with brine (100 mL), dried (Na_2SO_4) and concentrated *in vacuo*. Purification of the residue by flash column chromatography (2 x 14 cm, silica, *n*-pentane : Et_2O = 3 : 1, 20 mL, #17─27) afforded twistanol **592** (189 mg, 93%) as a colorless solid.

$C_{10}H_{16}O$ M_r = 152.24 g·mol^{-1}.

TLC R_f = 0.55 (hexanes : EtOAc = 3 : 1).

mp 213 – 215 °C.

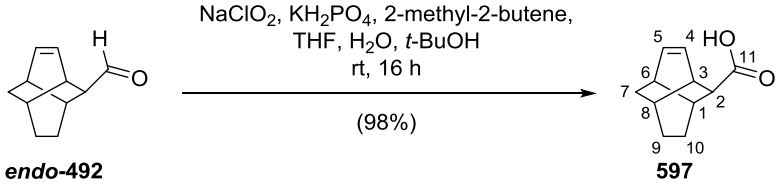
^{1}H NMR (400 MHz, $CDCl_3$): δ = 3.93 (d, $^3J_{C2\text{-}H,C1\text{-}H}$ = 6.1 Hz, 1H, C2-H), 1.99 – 1.92 (m, 1H, C1-H*), 1.86 – 1.71 (m, 4H, C3-H*, C4-H_A**, C5-H_A**, C6-H*), 1.60 – 1.37 (m, 7H, C4-H_B**, C5-H_B**, C7-H_A**, C8-H*, C9-H_A**, C10-H**), 1.37 – 1.29 (m, 1H, C9-H_B**), 1.28 – 1.21 (m, 1H, C7-H_B**) ppm.

^{13}C NMR (100 MHz, $CDCl_3$): δ = 72.6 (C2), 36.9 (C8*), 34.3 (C1*), 29.8 (C3*), 29.2 (C6*), 28.1 (C7**), 25.5 (C5**), 24.5 (C9**), 24.3 (C10**), 18.1 (C4**) ppm.

IR (ATR): $\tilde{\nu}$ = 3271 (vw), 2918 (s), 2866 (m), 1483 (vw), 1465 (w), 1367 (vw), 1339 (vw), 1328 (vw), 1302 (vw), 1230 (vw), 1159 (vw), 1131 (vw), 1081 (m), 1061 (w), 1036 (w), 1019 (w), 985 (vw), 943 (vw), 906 (s), 877 (vw), 842 (vw), 809 (w), 731 (vs), 712 (m) cm^{-1}.

HRMS (EI): m/z for $C_{10}H_{16}O^+$ $[M]^+$: calcd.: 152.1196
found: 152.1198.

Tricyclo[4.4.0.0^{3,8}]dec-4-ene-2-*endo*-carboxylic acid (597)



To a solution of aldehyde ***endo*-492** (32.4 mg, 0.200 mmol, 1.00 eq.) and KH_2PO_4 (272 mg, 2.00 mmol, 10.0 eq.) in THF : H_2O : *t*-BuOH (4 : 4 : 1, 45.0 mL) was added 2-methyl-2-butene (5.00 mL, 3.30 g, 47.1 mmol, 235 eq.) and $NaClO_2$ (113 mg, 1.00 mmol, 5.00 eq.). The resulting mixture was stirred at room temperature for 16 h. The reaction mixture was diluted with saturated aqueous NH_4Cl (45 mL) and extracted with EtOAc (3 x 100 mL). The combined organic layer was washed with brine (50 mL), dried (Na_2SO_4) and concentrated *in vacuo* to afford carboxylic acid **597** (35 mg, 98%) as a colorless solid.

$C_{11}H_{14}O_2$ M_r = 178.23 g·mol^{-1}.

TLC R_f = 0.14 (hexanes : EtOAc = 9 : 1).

mp 98 – 100 °C.

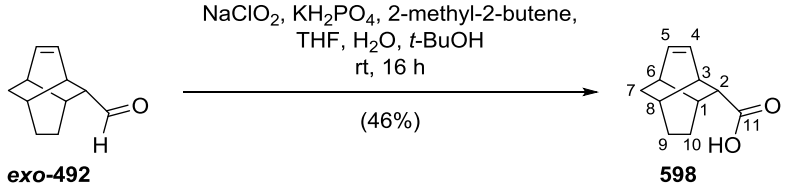
^{1}H-NMR (600 MHz, $CDCl_3$): δ = 6.44 (ddd, $^3J_{C5\text{-}H,C4\text{-}H}$ = 7.8 Hz, $^3J_{C5\text{-}H,C6\text{-}H}$ = 6.4 Hz, $^4J_{C5\text{-}H,C3\text{-}H}$ = 1.4 Hz, 1H, C5-H), 6.05 (ddd, $^3J_{C4\text{-}H,C5\text{-}H}$ = 7.8 Hz, $^3J_{C4\text{-}H,C3\text{-}H}$ = 6.0 Hz, $^4J_{C4\text{-}H,C6\text{-}H}$ = 1.4 Hz, 1H, C4-H), 3.12 – 3.08 (m, 1H, C3-H), 2.82 (d, $^3J_{C2\text{-}H,C3\text{-}H}$ = 5.3 Hz, 1H, C2-H), 2.65 – 2.60 (m, 1H, C6-H), 2.09 – 2.05 (m, 1H, C1-H), 1.77 – 1.57 (m, 6H, C7-H_A, C8-H, C9-H, C10-H), 1.01 (ddd, $^2J_{C7\text{-}H_B,C7\text{-}H_A}$ = 11.3 Hz, $^3J_{C7\text{-}H_B,C6\text{-}H}$ = 6.8 Hz, $^2J_{C7\text{-}H_B,C8\text{-}H}$ = 2.5 Hz, 1H, C7-H_B) ppm.

^{13}C-NMR (150 MHz, $CDCl_3$): δ = 178.9 (C11), 138.3 (C5), 129.7 (C4), 49.8 (C2), 37.1 (C3), 36.3 (C7), 33.9 (C6), 26.5 (C1), 25.2 (C9), 24.5 (C10), 23.6 (C8) ppm.

IR (ATR): $\tilde{\nu}$ = 3049 (w), 2956 (s), 2878 (m), 1702 (vs), 1480 (vw), 1462 (vw), 1452 (vw), 1417 (w), 1356 (vw), 1320 (vw), 1292 (vw), 1270 (vw), 1255 (m), 1234 (vw), 1206 (vw), 1184 (vw), 1135 (vw), 1113 (vw), 1078 (vw), 1049 (vw), 930 (vw), 882 (vw), 862 (vw), 848 (vw), 812 (vw), 794 (vw), 753 (vw), 688 (w), 674 (w), 644 (vw), 624 (vw), 617 (vw) cm^{-1}.

HRMS (EI): m/z for $C_{11}H_{14}O_2^+$ $[M]^+$: calcd.: 178.0988
found: 178.0978.

Tricyclo[4.4.0.0^{3,8}]dec-4-ene-2-*exo*-carboxylic acid (598)



To a solution of aldehyde ***exo*-492** (281 mg, 1.73 mmol, 1.00 eq.) and KH_2PO_4 (2.35 g, 17.3 mmol, 10.0 eq.) in THF : H_2O : *t*-BuOH (4 : 4 : 1, 113 mL) was added 2-methyl-2-butene (10.0 mL, 6.60 g, 94.1 mmol, 54.4 eq.) and $NaClO_2$ (978 mg, 8.65 mmol, 5.00 eq.). The resulting mixture was stirred at room temperature for 16 h. The reaction mixture was diluted with saturated aqueous NH_4Cl (100 mL) and extracted with EtOAc (3 x 100 mL). The combined organic layer was washed with brine (100 mL), dried (Na_2SO_4) and concentrated *in vacuo* to afford carboxylic acid **598** (141 mg, 46%) as a colorless solid.

$C_{11}H_{14}O_2$ M_r = 178.23 g·mol^{-1}.

TLC R_f = 0.12 (hexanes : EtOAc = 9 : 1).

mp 133 – 135 °C.

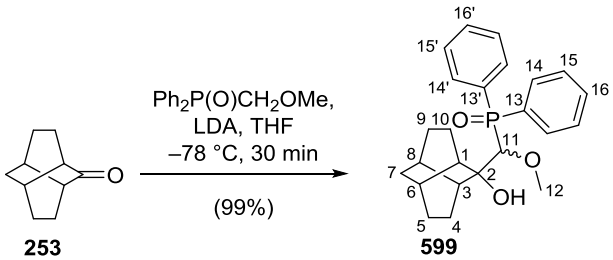
^{1}H-NMR (300 MHz, $CDCl_3$): δ = 6.40 – 6.28 (m, 2H, C4-H, C5-H), 3.13 – 3.02 (m, 1H, C3-H), 2.73 – 2.60 (m, 1H, C6-H), 2.29 – 2.20 (m, 1H, C2-H), 2.01 – 1.91 (m, 1H, C1-H), 1.91 – 1.47 (m, 6H, C7-H_A, C8-H, C9-H, C10-H), 1.09 – 0.99 (m, 1H, C7-H_B) ppm.

^{13}C-NMR (75 MHz, $CDCl_3$): δ = 180.7 (C11), 136.3 (C5), 135.7 (C4), 53.5 (C2), 36.9 (C7), 35.7 (C3), 35.3 (C6), 25.5 (C1), 24.5 (C9), 22.5 (C8), 20.5 (C10) ppm.

IR (ATR): $\tilde{\nu}$ = 3042 (w), 2936 (s), 2883 (m), 1698 (vs), 1462 (w), 1410 (w), 1352 (w), 1328 (w), 1272 (w), 1248 (w), 1195 (w), 1074 (w), 968 (w), 786 (w), 690 (w) cm^{-1}.

HRMS (EI): m/z for $C_{11}H_{14}O_2^+$ $[M]^+$: calcd.: 178.0988
found: 178.0980.

((2-Hydroxytricyclo[4.4.0.0^{3,8}]decan-2-yl)(methoxy)methyl)diphenylphosphine oxide (599)



To a solution of diisopropylamine (3.07 mL, 2.20 g, 21.7 mmol, 5.44 eq.) in THF (35.0 mL) at 0 °C was added *n*-butyllithium (2.6 M in hexanes, 7.67 mL, 19.9 mmol, 5.00 eq.) and the resulting mixture was stirred at 0 °C for 20 min. To the mixture was added a solution of

methoxymethyldiphenylphosphine oxide (5.90 g, 23.9 mmol, 6.00 eq.) in THF (55.0 mL). The resulting solution was stirred at 0 °C for 15 min and was then cooled to ─78 °C. At ─78 °C a solution of ketone **253** (0.600 g, 3.99 mmol, 1.00 eq.) in THF (35.0 mL) was added dropwise and the resulting mixture was stirred at ─78 °C for 30 min. The reaction was quenched by addition of saturated aqueous NH_4Cl, warmed to room temperature and the aqueous layer was extracted with Et_2O (3 x 60 mL). The combined organic layer was dried (Na_2SO_4) and concentrated *in vacuo*. Purification of the residue by flash column chromatography (5 x 5 cm, silica, hexanes : EtOAc = 1 : 1, 100 mL, #4─9) afforded the desired phosphine oxide **599** (1.56 g, 99%) as a colorless solid.

$C_{24}H_{29}O_3P$ M_r = 396.47 g·mol^{-1}.

TLC R_f = 0.41 (hexanes : EtOAc = 1 : 1).

mp 162 – 165 °C.

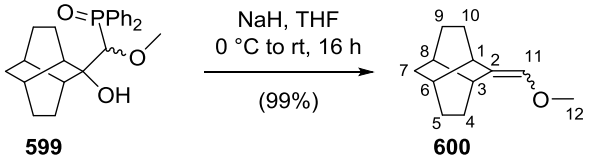
^{1}H NMR (600 MHz, $CDCl_3$): δ = 7.95 – 7.89 (m, 2H, C14-H), 7.83 – 7.77 (m, 2H, C14-H'), 7.63 – 7.56 (m, 3H, C15-H, C16-H), 7.53 – 7.49 (m, 1H, C16-H'), 7.46 – 7.41 (m, 2H, C15-H'), 4.42 (d, $^2J_{C11\text{-}H,P}$ =3.2 Hz, 1H, C11-H), 2.99 (s, 3H, C12-H), 2.28 – 2.21 (m, 1H, C4-H_A*), 2.04 – 1.99 (m, 1H, C1-H**), 1.91 – 1.83 (m, 2H, C3-H**, C5-H_A*), 1.80 – 1.74 (m, 1H, C6-H**), 1.68 – 1.60 (m, 1H, C7-H_A**), 1.60 – 1.52 (m, 3H, C7-H_B*, C8-H**, C9-H_A*), 1.44 – 1.37 (m, 1H, C9-H_B*), 1.37 – 1.29 (m, 2H, C5-H_B*, C10-H_A*), 1.27 – 1.19 (m, 2H, C4-H_B*, C10-H_B*) ppm.

^{13}C NMR (150 MHz, $CDCl_3$): δ = 132.3 (d, $^1J_{C13,P}$ = 89.9 Hz, C13), 132.3 (d, $^2J_{C14,P}$ = 9.0 Hz, C14'), 132.2 (C16), 132.0 (C16') , 131.6 (d, $^2J_{C14,P}$ = 9.0 Hz, C14), 131.3 (d, $^1J_{C13,P}$ = 89.9 Hz, C13'), 129.0 (d, $^3J_{C15,P}$ = 11.5 Hz, C15), 128.4 (d, $^3J_{C15,P}$ = 11.5 Hz, C15'), 86.4 (d, $^1J_{C11,P}$ = 80.2 Hz, C15), 80.3 (C2), 60.1 (C12), 37.6 (C6**), 35.7 (C1**), 30.8 (C3**), 30.4 (C10*), 30.1 (C8**), 27.6 (C4*), 27.0 (C9*), 22.0 (C7*), 21.6 (C5*) ppm.

IR (ATR): $\tilde{\nu}$ = 3350 (vw), 3057 (vw), 2930 (m), 2881 (w), 2827 (vw), 2236 (vw), 1590 (vw), 1490 (vw), 1473 (vw), 1462 (vw), 1437 (m), 1313 (vw), 1156 (m), 1115 (m), 1084 (s), 1037 (vw), 1028 (vw), 996 (w), 928 (w), 908 (w), 872 (vw), 844 (vw), 769 (vw), 724 (vs), 695 (vs) cm^{-1}.

HRMS (EI): m/z for $C_{24}H_{29}O_3P^+$ $[M]^+$: calcd.: 396.1849
found: 396.1859.

2-(Methoxymethylene)tricyclo[4.4.0.0^{3,8}]decane (600)



599 **600**

To a solution of phosphine oxide **599** (1.56 g, 3.97 mmol, 1.00 eq.) in THF (170 mL) at 0 °C was added NaH (60 wt-%, 0.908 g, 22.7 mmol, 5.71 eq.) in portions. The resulting mixture was stirred at room temperature for 16 h. The mixture was cooled to 0 °C and quenched by addition of H_2O (10 mL). The mixture was extracted with Et_2O (3 x 25 mL) and the combined organic layer was dried (Na_2SO_4) and concentrated *in vacuo*. Purification of the residue by column chromatography (4 x 7 cm, silica, *n*-pentane : Et_2O = 98 : 2, 20 mL, #4─6) afforded enol ether **600** (705 mg, 99%) as a colorless oil.

$C_{12}H_{18}O$ M_r = 178.27 g·mol^{-1}.

TLC R_f = 0.66 (hexanes : EtOAc = 9 : 1).

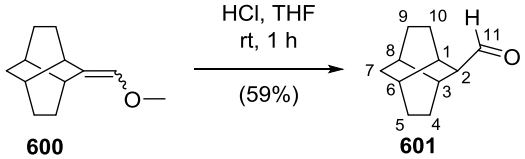
^{1}H NMR (400 MHz, DMSO-d_6): δ = 5.77 – 5.72 (m, 1H, C11-H), 3.43 (s, 3H, C12-H), 2.55 – 2.51 (m, 1H, C1-H*), 2.07 – 2.02 (m, 1H, C3-H*), 1.86 – 1.77 (m, 2H, C6-H*, C8-H*), 1.71 – 1.51 (m, 2H, C4-H_A**, C5-H_A**), 1.44 – 1.30 (m, 8H, C4-H_B**, C5-H_B**, C7-H, C9-H, C10-H) ppm.

^{13}C NMR (100 MHz, DMSO-d_6): δ = 136.5 (C11), 123.0 (C2), 58.7 (C12), 34.1 (C3*), 31.8 (C1*), 29.3 (C6*), 29.2 (C8*), 26.6 (C7**), 25.9 (C4**), 25.3 (C9**), 25.3 (C10*), 23.4 (C5**) ppm.

IR (ATR): $\tilde{\nu}$ = 2926 (s), 2859 (m), 2830 (vw), 1695 (w), 1478 (vw), 1460 (w), 1442 (vw), 1366 (vw), 1225 (m), 1187 (m), 1120 (vs), 1082 (vw), 1067 (vw), 1012 (vw), 979 (vw), 872 (vw), 836 (vw), 826 (vw), 791 (vw), 741 (vw) cm^{-1}.

HRMS (EI): m/z for $C_{12}H_{18}O^+$ $[M]^+$: calcd.: 178.1352
found: 178.1352.

Tricyclo[4.4.0.0^{3,8}]decane-2-carbaldehyde (601)



600 **601**

To a solution of methyl enol ether **600** (713 mg, 4.00 mmol, 1.00 eq.) in THF (100 mL) was added 3 M HCl (50.0 mL) and the resulting mixture was stirred at room temperature for 1 h. The mixture was treated with solid $NaHCO_3$ until a neutral pH was observed and was then extracted with CH_2Cl_2 (3 x 100 mL). The combined organic layer was dried (Na_2SO_4) and concentrated *in vacuo*. Purification of

the residue by flash column chromatography (4 x 10 cm, silica, *n*-pentane : Et_2O = 95 : 5, 20 mL, #9─16) afforded aldehyde **601** (388 mg, 59%) as a colorless waxy solid.

$C_{11}H_{16}O$ M_r = 164.25 g·mol^{-1}.

TLC R_f = 0.49 (hexanes : EtOAc = 9 : 1).

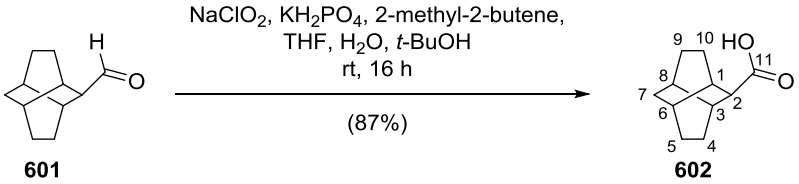
^{1}H NMR (400 MHz, $CDCl_3$): δ = 9.88 (s, 1H, C11-H), 2.31 – 2.22 (m, 2H, C1-H*, C3-H*), 2.17 (d, $^3J_{C2\text{-}H,C1\text{-}H}$ = 5.6 Hz, 1H, C2-H), 1.89 – 1.82 (m, 1H, C6-H*), 1.82 – 1.77 (m, 1H, C8-H*), 1.70 – 1.41 (m, 7H, C4-H**, C5-H**, C7-H**, C9-H_A**), 1.40 – 1.28 (m, 2H, C10-H**), 1.26 – 1.15 (m, 1H, C9-H_B**) ppm.

^{13}C NMR (100 MHz, $CDCl_3$): δ = 206.2 (C11), 51.7 (C2), 30.5 (C1*), 29.0 (C3*), 28.7 (C6*), 28.5 (C8*), 28.0 (C10**), 24.7 (C4**), 24.6 (C5**), 24.6 (C9**), 19.6 (C7**) ppm.

IR (ATR): $\tilde{\nu}$ = 2921 (vs), 2868 (m), 2853 (m), 2693 (vw), 1718 (m), 1467 (w), 1377 (vw), 1228 (vw), 1099 (vw), 1086 (vw), 1004 (vw), 899 (vw), 714 (vw) cm^{-1}.

HRMS (EI): m/z for $C_{11}H_{16}O^+$ $[M]^+$: calcd.: 164.1196
found: 164.1204.

Tricyclo[4.4.0.0^{3,8}]decane-2-carboxylic acid (602)



601 **602**

To a solution of aldehyde **601** (50.1 mg, 0.305 mmol, 1.00 eq.) and KH_2PO_4 (415 g, 3.05 mmol, 10.0 eq.) in THF : H_2O : *t*-BuOH (4 : 4 : 1, 68.6 mL) was added 2-methyl-2-butene (7.63 mL, 5.03 g, 71.8 mmol, 235 eq.) and $NaClO_2$ (172 mg, 1.52 mmol, 5.00 eq.). The resulting mixture was stirred at room temperature for 16 h. The reaction mixture was diluted with saturated aqueous NH_4Cl (50 mL) and extracted with EtOAc (3 x 50 mL). The combined organic layer was washed with brine (50 mL), dried (Na_2SO_4) and concentrated *in vacuo* to afford carboxylic acid **602** (48 mg, 87%) as a colorless solid.

$C_{11}H_{16}O_2$ M_r = 180.25 g·mol^{-1}.

mp 95 – 98 °C.

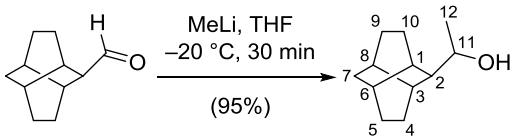
^{1}H NMR (600 MHz, $CDCl_3$): δ = 2.49 – 2.46 (m, 1H, C2-H), 2.27 – 2.22 (m, 1H, C3-H), 2.19 – 2.14 (m, 1H, C1-H), 1.88 – 1.82 (m, 1H, C6-H), 1.81 – 1.77 (m, 1H, C8-H), 1.78 – 1.72 (m, 1H, C10-H_A), 1.66 – 1.49 (m, 6H, C4-H, C5-H, C9-H_A, C10-H_B), 1.46 – 1.40 (m, 1H, C9-H_B), 1.39 – 1.35 (m, 1H, C7-H_A), 1.34 – 1.29 (m, 1H, C7-H_B) ppm.

^{13}C NMR (150 MHz, $CDCl_3$): δ = 180.3 (C11), 43.8 (C2), 31.5 (C1), 29.7 (C3), 29.1 (C6), 28.2 (C7), 28.2 (C8), 24.9 (C4), 24.9 (C5), 24.3 (C9), 20.3 (C10) ppm.

IR (ATR): $\tilde{\nu}$ = 2932 (vs), 2873 (s), 2360 (w), 2340 (w), 1696 (vs), 1469 (vw), 1456 (vw), 1412 (w), 1335 (vw), 1254 (w), 1221 (w), 1070 (vw), 923 (vw), 884 (vw), 773 (vw), 749 (vw), 668 (w) cm^{-1}.

HRMS (ESI–): m/z for $C_{11}H_{15}O_2^-$ $[M–H]^-$: calcd.: 179.1078
found: 179.1075.

1-(Tricyclo[4.4.0.0^{3,8}]decan-2-yl)ethan-1-ol (606)



601 **606**

To a solution of aldehyde **601** (460 mg, 2.80 mmol, 1.00 eq.) in THF (50.0 mL) at –20 °C was added a solution of MeLi LiBr in Et_2O (1.48 M, 5.68 mL, 8.40 mmol, 3.00 eq.). The reaction mixture was allowed to warm to room temperature and stirred at this temperature for 30 min. The solution was re-cooled to 0 °C and the reaction was quenched by addition of saturated aqueous NH_4Cl. (50 mL). The mixture was diluted with H_2O (50 mL) and CH_2Cl_2 (50 mL). The organic layer was separated and the aqueous layer was extracted with CH_2Cl_2 (3 x 75 mL). The combined organic layer was dried (Na_2SO_4) and concentrated *in vacuo* to afford alcohol **606** (480 mg, 95%) as an inconsequential diastereomeric mixture in form of a colorless oil. The crude material was used in the next step without further purification.

$C_{12}H_{20}O$ M_r = 180.29 g·mol^{-1}.

TLC R_f = 0.15 (hexanes : EtOAc = 9 : 1).

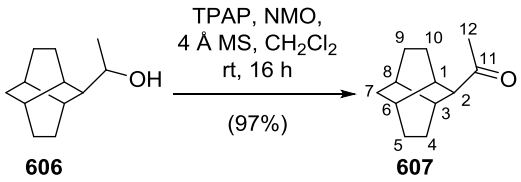
^{1}H NMR (400 MHz, $CDCl_3$, both diastereomers): δ = 3.97 – 3.79 (m, 1H, C11-H), 1.92 – 1.23 (m, 15H, C1-H, C2-H, C3-H, C4-H, C5-H, C6-H, C7-H, C8-H, C9-H, C10-H), 1.21 – 1.12 (m, 3H, C12-H) ppm.

^{13}C NMR (100 MHz, $CDCl_3$, both diastereomers): δ = 70.4 , 69.8, 48.3, 48.1, 30.9, 30.6, 29.7, 29.6, 29.5, 29.5, 29.2, 29.1, 29.1, 28.9, 26.5, 26.5, 26.4, 26.0, 24.7, 24.6, 23.1, 22.2, 19.2, 18.7 ppm.

IR (ATR): $\tilde{\nu}$ = 3335 (w), 2923 (vs), 2869 (s), 1706 (vw), 1484 (w), 1468 (m), 1454 (w), 1369 (w), 1332 (w), 1291 (vw), 1263 (vw), 1227 (vw), 1157 (w), 1128 (m), 1094 (m), 1078 (m), 1064 (w), 1051 (s), 1027 (m), 987 (w), 935 (vw), 905 (m), 877 (m), 838 (w), 812 (vw), 794 (vw), 767 (vw) cm^{-1}.

HRMS (EI): m/z for $C_{12}H_{20}O^+$ $[M]^+$: calcd.: 180.1509
found: 180.1502.

1-(Tricyclo[4.4.0.0^{3,8}]decan-2-yl)ethan-1-one (607)



To a solution of alcohol **606** (505 mg, 2.80 mmol, 1.00 eq.) in CH_2Cl_2 (50.0 mL) was added ground 4 Å molecular sieves (2.30 g) and NMO (656 mg, 5.60 mmol, 2.00 eq.). The solution was cooled to 0 °C and TPAP (49.2 mg, 0.140 mmol, 0.050 eq.) was added in one portion. The reaction mixture was stirred at room temperature for 16 h, after which time the solvent was removed *in vacuo*. The residue was purified by column chromatography (4 x 21 cm, silica, *n*-pentane : Et_2O = 9 : 1, 20 mL, #30–55) to afford ketone **607** (484 mg, 97%) as a colorless oil.

$C_{12}H_{18}O$ M_r = 178.27 g·mol^{-1}.

TLC R_f = 0.43 (hexanes : EtOAc = 9 : 1).

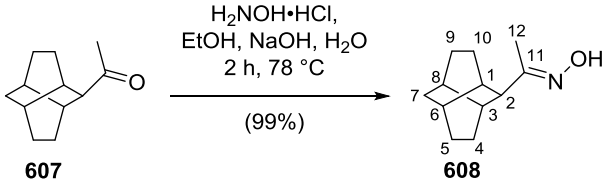
^{1}H NMR (400 MHz, $CDCl_3$): δ = 2.34 – 2.24 (m, 3H, C1-H*, C2-H*, C3-H*), 2.14 (s, 3H, C12-H), 1.91 – 1.84 (m, 1H, C6-H*), 1.81 – 1.74 (m, 1H, C8-H*), 1.67 – 1.28 (m, 10H, C4-H, C5-H, C7-H, C9-H, C10-H) ppm.

^{13}C NMR (100 MHz, $CDCl_3$): δ = 212.3 (C11), 53.6 (C2), 32.4 (C1*), 29.5 (C3*), 28.6 (C6*), 28.4 (C4**), 28.1 (C8*), 27.8 (C12), 25.1 (C5**), 24.8 (C7**), 24.1 (C9**), 20.4 (C10**) ppm.

IR (ATR): $\tilde{\nu}$ = 2929 (vs), 2869 (m), 1703 (vs), 1485 (vw), 1468 (w), 1452 (w), 1363 (w), 1349 (w), 1328 (vw), 1269 (vw), 1230 (w), 1206 (vw), 1185 (s), 1158 (vw), 1138 (vw), 1071 (vw), 1048 (vw), 1033 (vw), 996 (vw), 955 (vw), 927 (vw), 869 (vw), 830 (vw), 768 (vw) cm^{-1}.

HRMS (EI): m/z for $C_{12}H_{18}O^+$ $[M]^+$: calcd.: 178.1352
found: 178.1358.

1-(Tricyclo[4.4.0.0^{3,8}]decan-2-yl)ethan-1-one oxime (608)



607 608

To a solution of twistanone **607** (157 mg, 0.880 mmol, 1.00 eq.) in ethanol (1.75 mL) was added a solution of hydroxylamine hydrochloride (141 mg, 2.02 mmol, 2.30 eq.) in 2 M NaOH (0.660 mL). The resulting mixture was stirred for 2 h at 78 °C and was then allowed to cool to room temperature. The reaction mixture was concentrated *in vacuo* and the residue was diluted with water, which caused precipitation of a colorless solid. The mixture was extracted with CH_2Cl_2 (3 x 5 mL) and the combined organic layer was washed with H_2O (10 mL), dried (Na_2SO_4) and concentrated *in vacuo*. Purification of the residue by flash column chromatography (2 x 10 cm, silica, *n*-pentane : Et_2O = 1 : 1, 8 mL, #10–17) afforded the oxime **608** (170 mg, 99%) as a colorless solid.

$C_{12}H_{19}NO$ M_r = 193.29 g·mol^{-1}.

TLC R_f = 0.76 (hexanes : EtOAc = 3 : 1).

mp 160 – 161 °C.

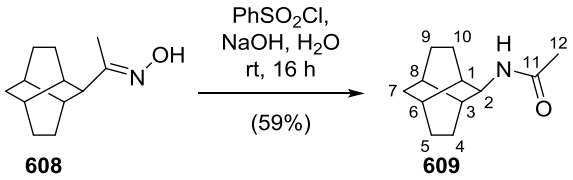
^{1}H NMR (600 MHz, $CDCl_3$): δ = 8.39 (s, 1H, OH), 2.31 – 2.25 (m, 2H, C1-H*, C2-H*), 2.07 – 2.02 (m, 1H, C3-H*), 1.90 – 1.82 (m, 5H, C4-H_A**, C6-H*, C12-H), 1.82 – 1.77 (m, 1H, C8-H*), 1.71 – 1.27 (m, 9H, C4-H_B**, C5-H**, C7-H**, C9-H**, C10-H**) ppm.

^{13}C NMR (150 MHz, $CDCl_3$): δ = 160.9 (C11), 45.5 (C1*), 31.9 (C2*), 29.6 (C3*), 29.2 (C4**), 29.0 (C6*), 28.2 (C8*), 25.4 (C5**), 25.0 (C7**), 24.4 (C9**), 20.0 (C10**), 13.0 (C12) ppm.

IR (ATR): $\tilde{\nu}$ = 3216 (w), 3164 (w), 2923 (vs), 2868 (vs), 1671 (vw), 1483 (w), 1465 (w), 1451 (w), 1364 (w), 1335 (vw), 1329 (vw), 1303 (vw), 1293 (vw), 1241 (w), 1233 (vw), 1159 (vw), 1067 (vw), 1036 (vw), 977 (m), 937 (w), 915 (s), 878 (w), 860 (w), 832 (w), 771 (w), 731 (m) cm^{-1}.

HRMS (EI): m/z for $C_{12}H_{19}NO^+$ $[M]^+$: calcd.: 193.1461
found: 193.1448.

***N*-(tricyclo[4.4.0.0^{3,8}]decan-2-yl)acetamide (609)**



To a solution of oxime **608** (89.3 mg, 0.462 mmol, 1.00 eq.) in 0.5 M NaOH (1.25 mL) at 0 °C was added benzenesulfonyl chloride (81 µL, 113 mg, 0.638 mmol, 1.38 eq.). The resulting mixture was stirred at room temperature for 16 h and was then neutralized with 0.5 M NaOH. The mixture was extracted with CH_2Cl_2 (10 x 5 mL) and the combined organic layer was dried (Na_2SO_4) and concentrated *in vacuo*. Purification of the residue by flash column chromatography (2 x 14 cm, silica, hexanes : EtOAc = 3 : 1, 8 mL, #38─74) afforded amide **609** (53 mg, 59%) as a colorless oil.

$C_{12}H_{19}NO$ M_r = 193.29 g·mol^{-1}.

TLC R_f = 0.24 (hexanes : EtOAc = 1 : 1).

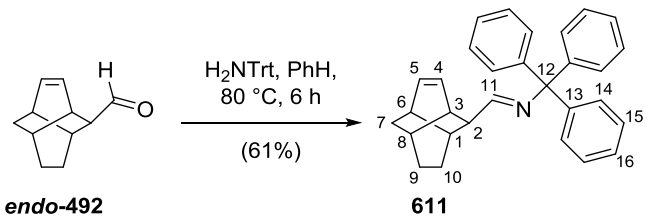
^{1}H NMR (400 MHz, $CDCl_3$): δ = 5.55 (s, 1H, N-H), 3.94 (dd, $^3J_{C2\text{-}H,N\text{-}H}$ = 6.6 Hz, $^3J_{C2\text{-}H,C1\text{-}H}$ = 6.6 Hz, 1H, C2-H), 2.08 – 2.02 (m, 1H, C1-H*), 1.98 (s, 3H, C12-H), 1.88 – 1.74 (m, 2H, C3-H*, C6-H*), 1.74 – 1.26 (m, 11H, C4-H, C5-H, C7-H, C8-H*, C9-H, C10-H) ppm.

^{13}C NMR (100 MHz, $CDCl_3$): δ = 169.6 (C11), 50.2 (C2), 35.0 (C8*), 31.5 (C1*), 29.1 (C3*), 28.9 (C6*), 28.3 (C4**), 25.8 (C5**), 24.9 (C7**), 24.1 (C12), 23.9 (C9**), 18.5 (C10**) ppm.

IR (ATR): $\tilde{\nu}$ = 3277 (s), 2916 (vs), 2869 (vs), 1629 (vs), 1543 (vs), 1482 (m), 1469 (m), 1454 (m), 1367 (s), 1341 (m), 1330 (m), 1308 (m), 1294 (m), 1284 (s), 1242 (m), 1234 (m), 1205 (w), 1166 (m), 1114 (m), 1072 (w), 1037 (m), 1018 (w), 998 (w), 977 (m), 960 (w), 938 (m), 915 (s), 878 (m), 861 (w), 833 (m), 733 (vs), 717 (vs) cm^{-1}.

HRMS (EI): m/z for $C_{12}H_{19}NO^+$ $[M]^+$: calcd.: 193.1461
found: 193.1464.

Tricyclo[4.4.0.0^{3,8}]dec-4-ene-2-syn-carbaldehyde *N*-tritylimine (611)



A solution of tritylamine (75.1 mg, 0.290 mmol, 0.950 eq.) and aldehyde ***endo*-492** (49.5 mg, 0.305 mmol, 1.00 eq.) in benzene (25.0 mL) was refluxed in a Dean-Stark apparatus over 3 Å

molecular sieves for 6 h. The reaction mixture was allowed to cool to room temperature and the solvent was removed *in vacuo*. Purification of the residue by recrystallization from MeOH afforded imine **611** (75 mg, 61%) as a colorless solid.

$C_{30}H_{29}N$ M_r = 403.57 g·mol^{-1}.

mp 122 °C (dec.).

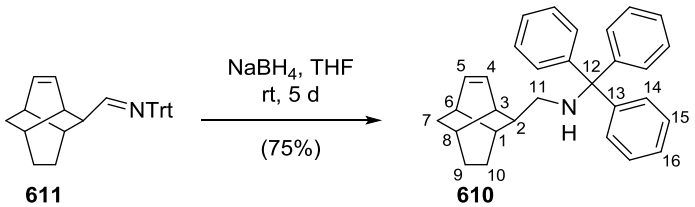
^{1}H NMR (400 MHz, $CDCl_3$): δ = 7.29 – 7.14 (m, 15H, C14-H, C15-H, C16-H), 7.03 (d, $^3J_{C11\text{-}H,C2\text{-}H}$ = 1.9 Hz, 1H, C11-H), 6.44 – 6.38 (m, 1H, C5-H), 5.77 – 5.68 (m, 1H, C4-H), 2.97 – 2.89 (m, 2H, C2-H, C3-H), 2.66 – 2.58 (m, 1H, C6-H), 2.43 – 2.35 (m, 1H, C1-H), 1.83 – 1.58 (m, 6H, C7-H_A, C8-H, C9-H, C10-H), 1.02 ─ 0.92 (m, 1H, C7-H_B) ppm.

^{13}C NMR (100 MHz, $CDCl_3$): δ = 167.5 (C11), 146.3 (C5), 140.1 (C4), 130.0 (C14*), 129.4 (C13), 127.6 (C15*), 126.6 (C16), 77.9 (C12), 50.8 (C2), 38.2 (C3), 36.7 (C7), 34.9 (C6), 29.2 (C1), 25.4 (C9**), 25.0 (C10**), 24.0 (C8) ppm.

IR (ATR): $\tilde{\nu}$ = 3054 (vw), 2926 (w), 2869 (w), 1792 (vw), 1717 (w), 1662 (vw), 1596 (vw), 1516 (vw), 1489 (w), 1445 (m), 1261 (vw), 1184 (vw), 1080 (vw), 1032 (w), 1001 (w), 947 (w), 909 (w), 757 (m), 731 (m), 699 (vs) cm^{-1}.

HRMS (EI): m/z for $C_{30}H_{28}N^+$ $[M–H]^+$: calcd.: 402.2216
found: 402.2216.

N-Trityltricyclo[4.4.0.0^{3,8}]dec-4-ene-2-*endo*-methylamine (610)



To a solution of imine **611** (40.4 mg, 0.100 mmol, 1.00 eq.) in THF at 0 °C was added $NaBH_4$ (7.6 mg, 0.200 mmol, 2.00 eq.) and the resulting mixture was allowed to warm to room temperature and stirred at this temperature for 16 h. The reaction was quenched by addition of 2 M NaOH (2 mL). The mixture was extracted with CH_2Cl_2 (3 x 10 mL) and the combined organic layer was washed with 2 M NaOH (15 mL), brine (15 mL), dried (Na_2SO_4) and concentrated *in vacuo*. Purification of the residue by flash column chromatography (2 x 15 cm, silica, hexanes : EtOAc = 3 : 1 to 1 : 1, 8 mL, #6–7) afforded the desired tritylamine **610** (30 mg, 75%) as a colorless oil.

$C_{30}H_{31}N$ M_r = 405.58 g·mol^{-1}.

TLC R_f = 0.61 (hexanes : EtOAc = 9 : 1).

^{1}H NMR (600 MHz, $CDCl_3$): δ = 7.47 – 7.44 (m, 6H, C14-H), 7.27 – 7.24 (m, 6H, C15-H), 7.19 – 7.14 (m, 3H, C16-H), 6.20 (ddd, $^3J_{C5\text{-}H,C4\text{-}H}$ = 7.9 Hz, $^3J_{C5\text{-}H,C6\text{-}H}$ = 6.4 Hz,

$^4J_{C5\text{-}H,C3\text{-}H}$ = 1.4 Hz, 1H, C5-H), 5.64 (ddd, $^3J_{C4\text{-}H,C5\text{-}H}$ = 7.9 Hz, $^3J_{C4\text{-}H,C3\text{-}H}$ = 6.3 Hz, $^4J_{C4\text{-}H,C6\text{-}H}$ = 1.5 Hz, 1H, C4-H), 2.75 – 2.71 (m, 1H, C3-H), 2.40 – 2.35 (m, 1H, C6-H), 2.11 – 2.04 (m, 1H, C2-H), 1.90 (dd, $^2J_{C11\text{-}Ha,C11\text{-}Hb}$ = 11.3 Hz, $^3J_{C11\text{-}Ha,C2\text{-}H}$ = 6.4 Hz, 1H, C11-H_A), 1.84 – 1.76 (m, 2H, C9-H_A, C11-H_B), 1.66 – 1.58 (m, 2H, C7-H_A, C10-H_A), 1.58 – 1.49 (m, 3H, C8-H, C9-H_B, C10-H_B), 1.12 – 1.07 (m, 1H, C1-H), 0.94 – 0.89 (m, 1H, C7-H_B) ppm.

^{13}C NMR (150 MHz, $CDCl_3$): δ = 146.6 (C13), 137.6 (C5), 128.8 (C14), 127.7 (C15), 126.7 (C4), 126.2 (C16), 70.8 (C12), 45.8 (C11), 44.2 (C2), 37.3 (C3), 36.8 (C7), 34.6 (C6), 29.0 (C1), 25.7 (C10), 24.9 (C9), 24.1 (C8) ppm.

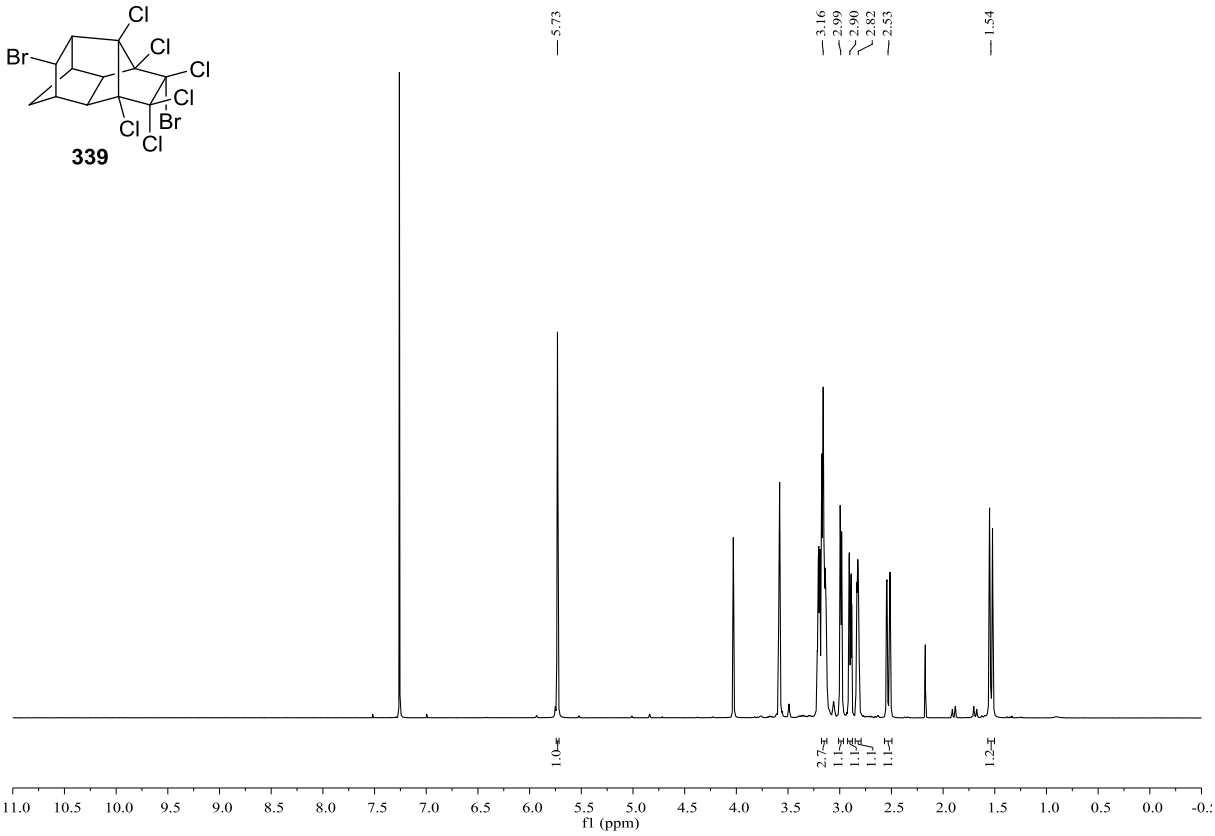
IR (ATR): $\tilde{\nu}$ = 3052 (vw), 2926 (s), 2874 (w), 1595 (vw), 1488 (w), 1448 (w), 1360 (vw), 1207 (vw), 1107 (vw), 1033 (vw), 899 (vw), 848 (vw), 828 (vw), 773 (w), 741 (w), 706 (vs), 698 (m) cm^{-1}.

HRMS (EI): m/z for $C_{30}H_{31}N^+$ $[M]^+$: calcd.: 405.2451
found: 405.2457.

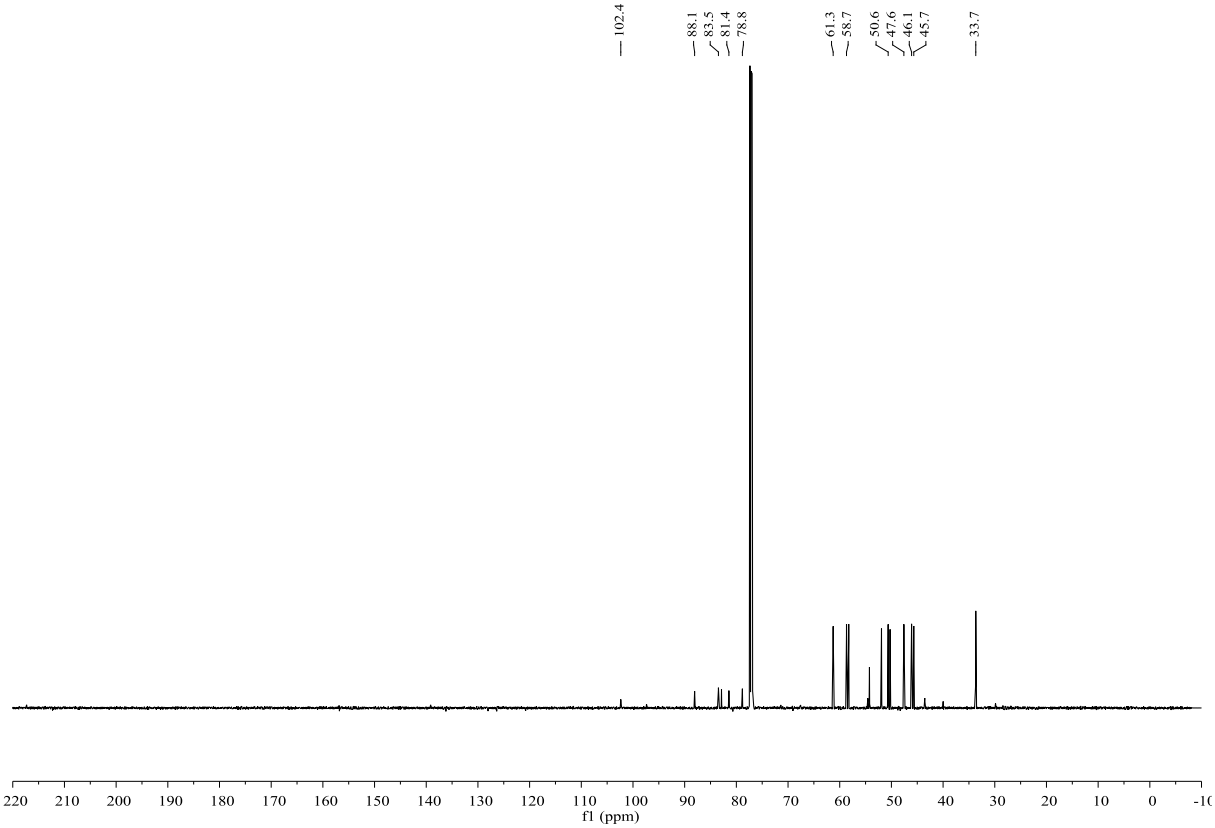
APPENDICES

8 NMR Spectra

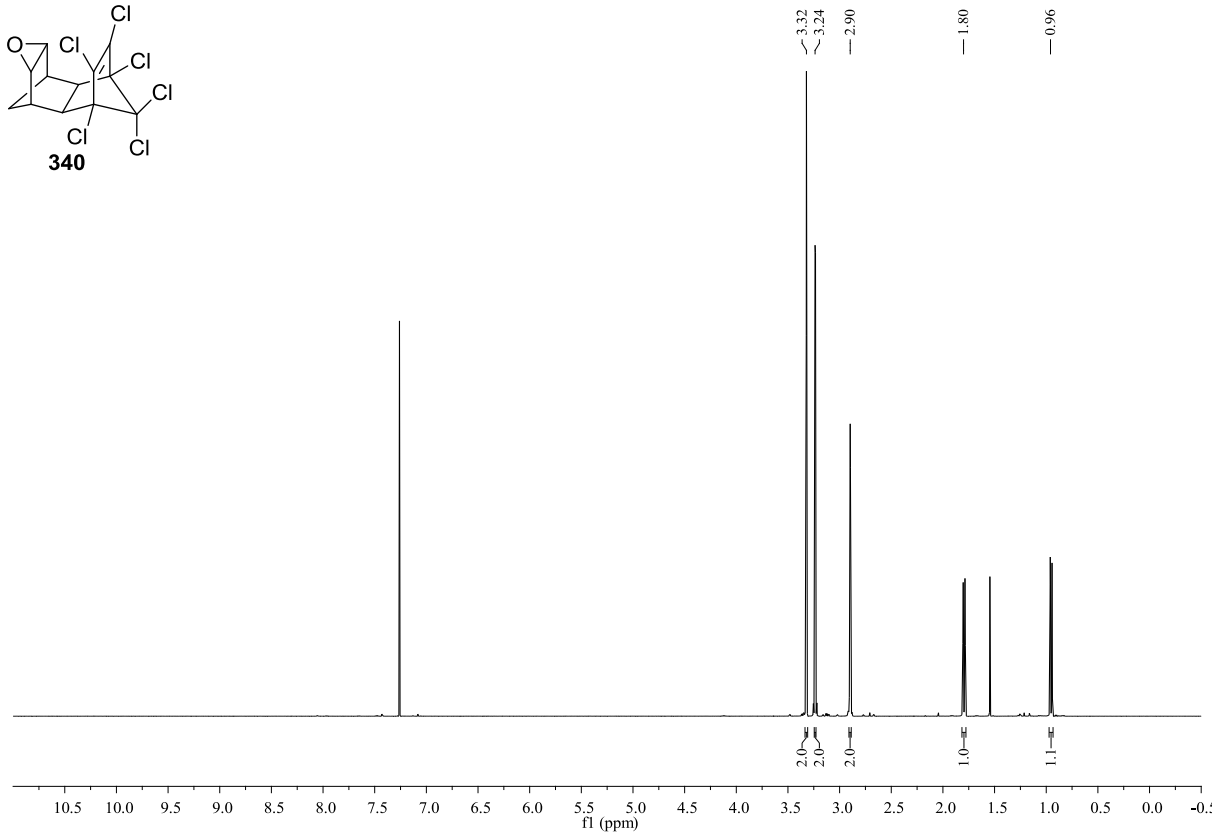
339 (^{1}H NMR, 400 MHz, $CDCl_3$)



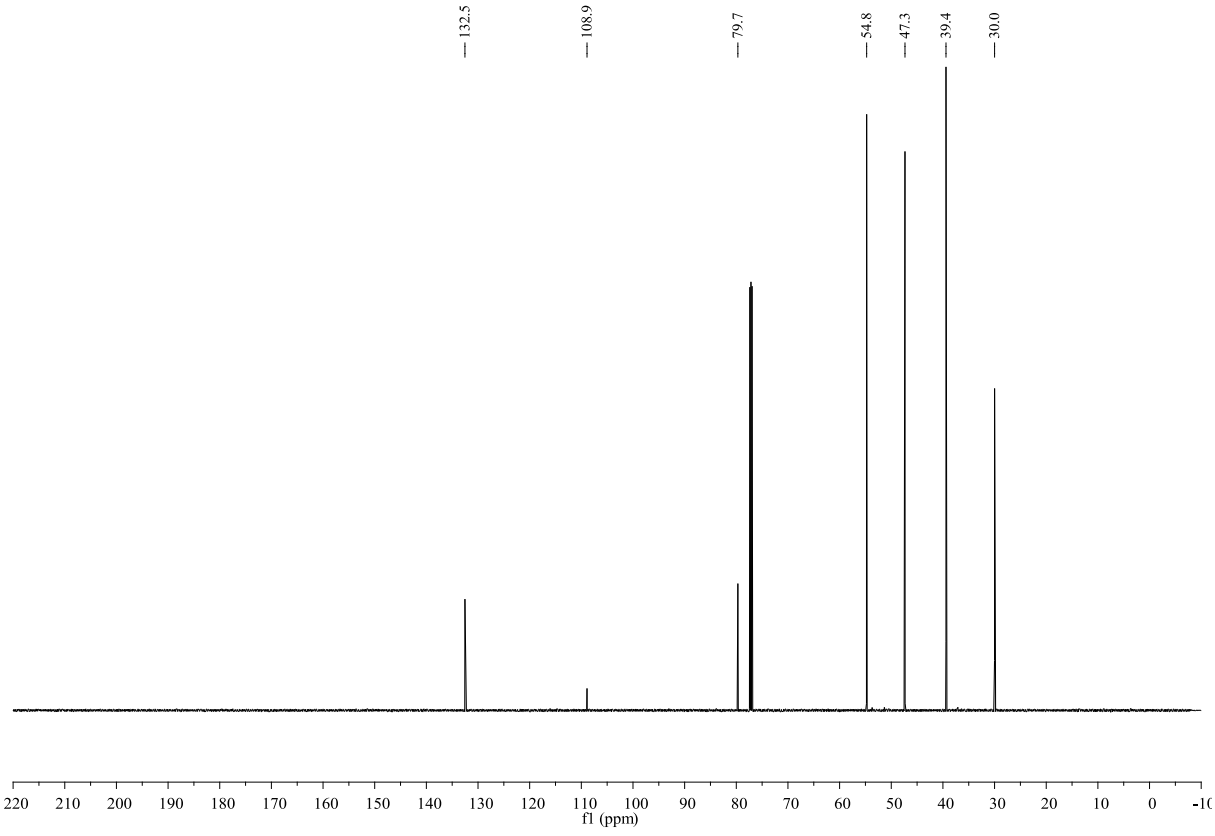
339 (^{13}C NMR, 150 MHz, $CDCl_3$)



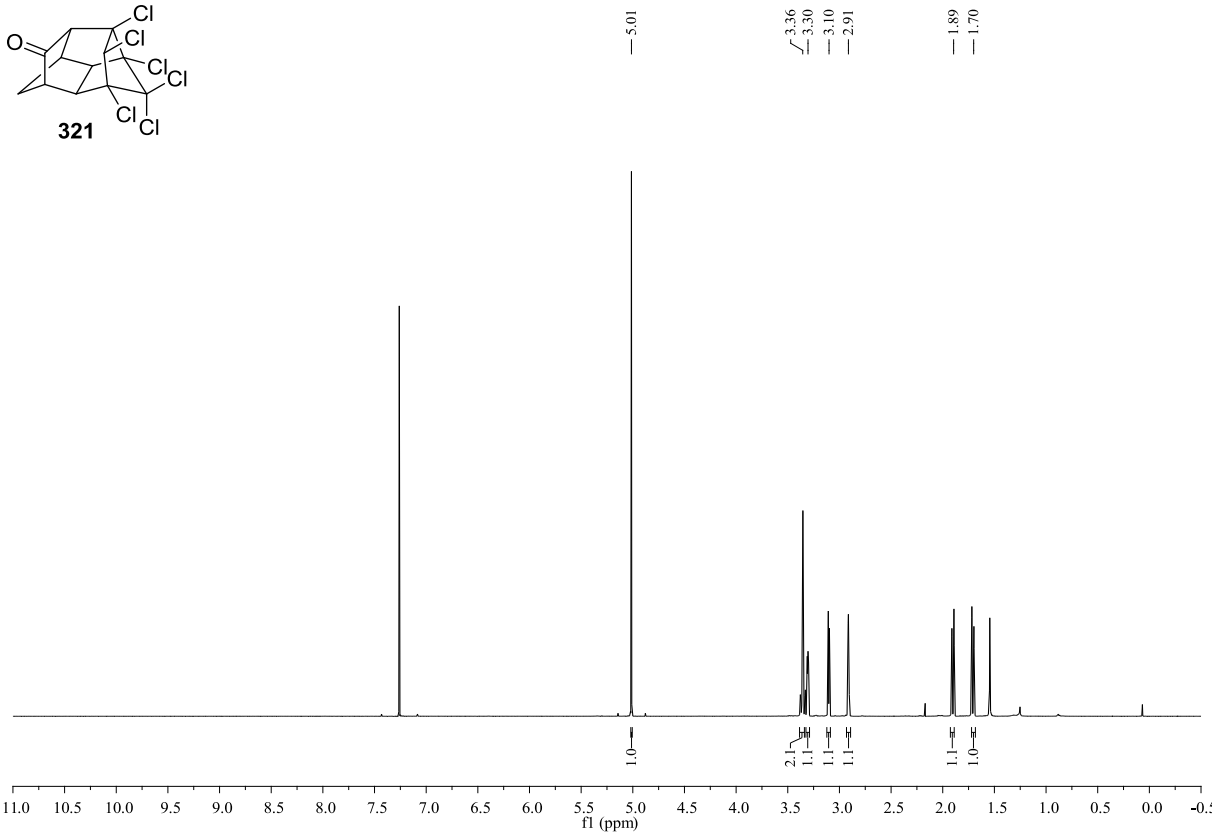
340 (^{1}H NMR, 600 MHz, $CDCl_3$)



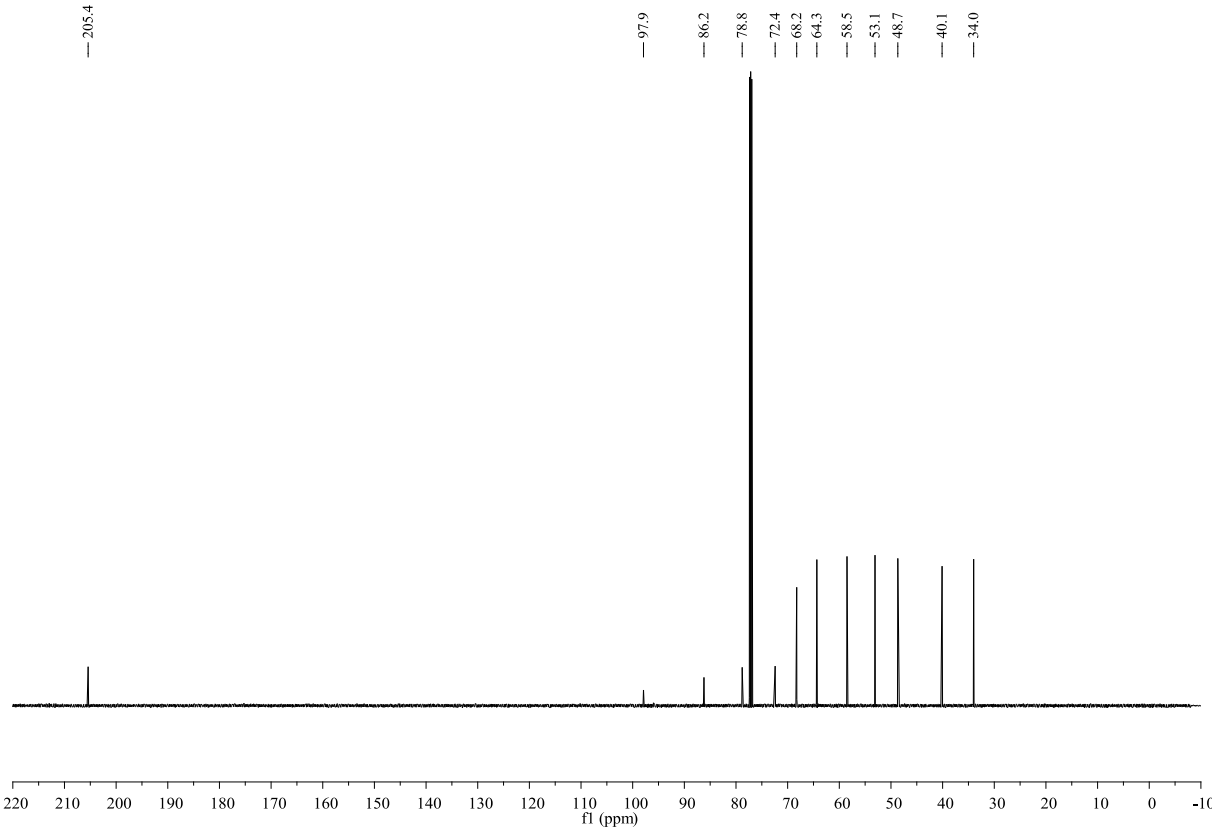
340 (^{13}C NMR, 150 MHz, $CDCl_3$)



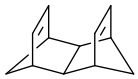
321 (^{1}H NMR, 600 MHz, $CDCl_3$)



321 (^{13}C NMR, 150 MHz, $CDCl_3$)

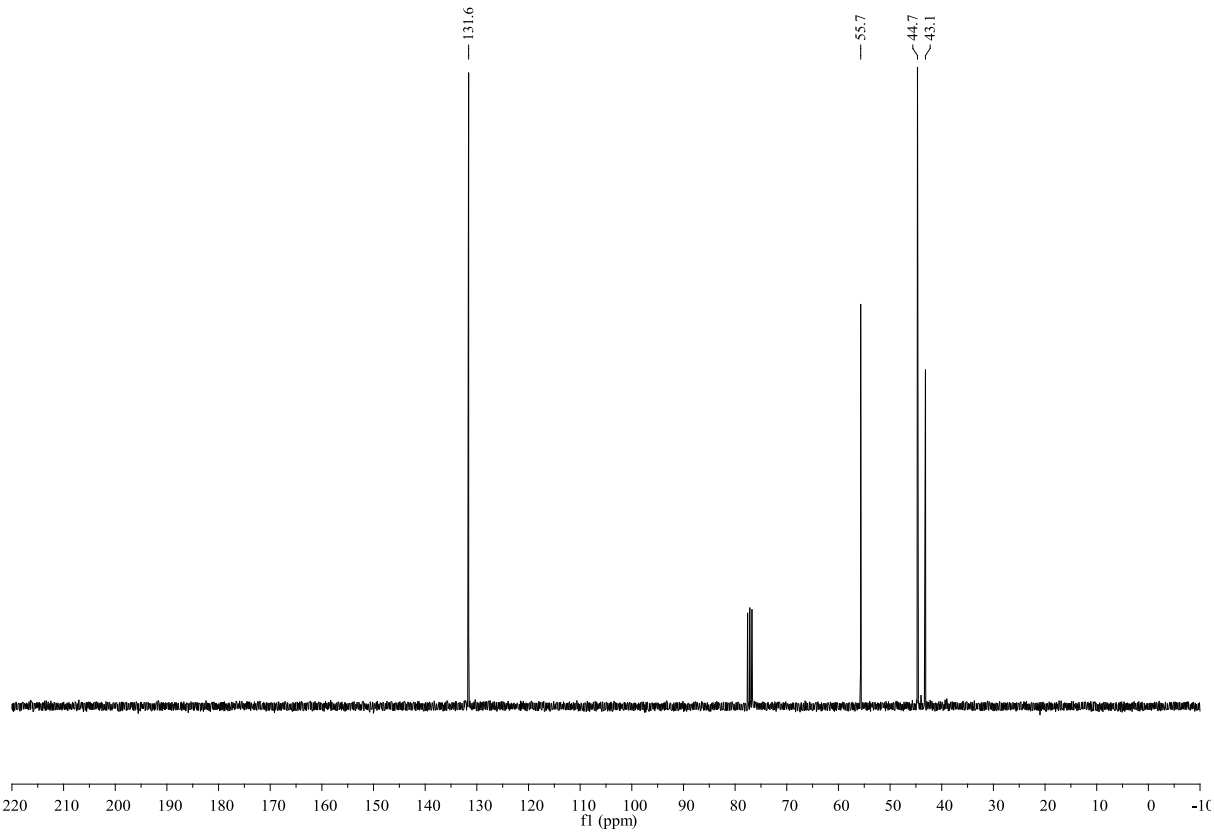


326 (^{1}H NMR, 300 MHz, $CDCl_3$)

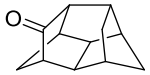


326

326 (^{13}C NMR, 75 MHz, $CDCl_3$)

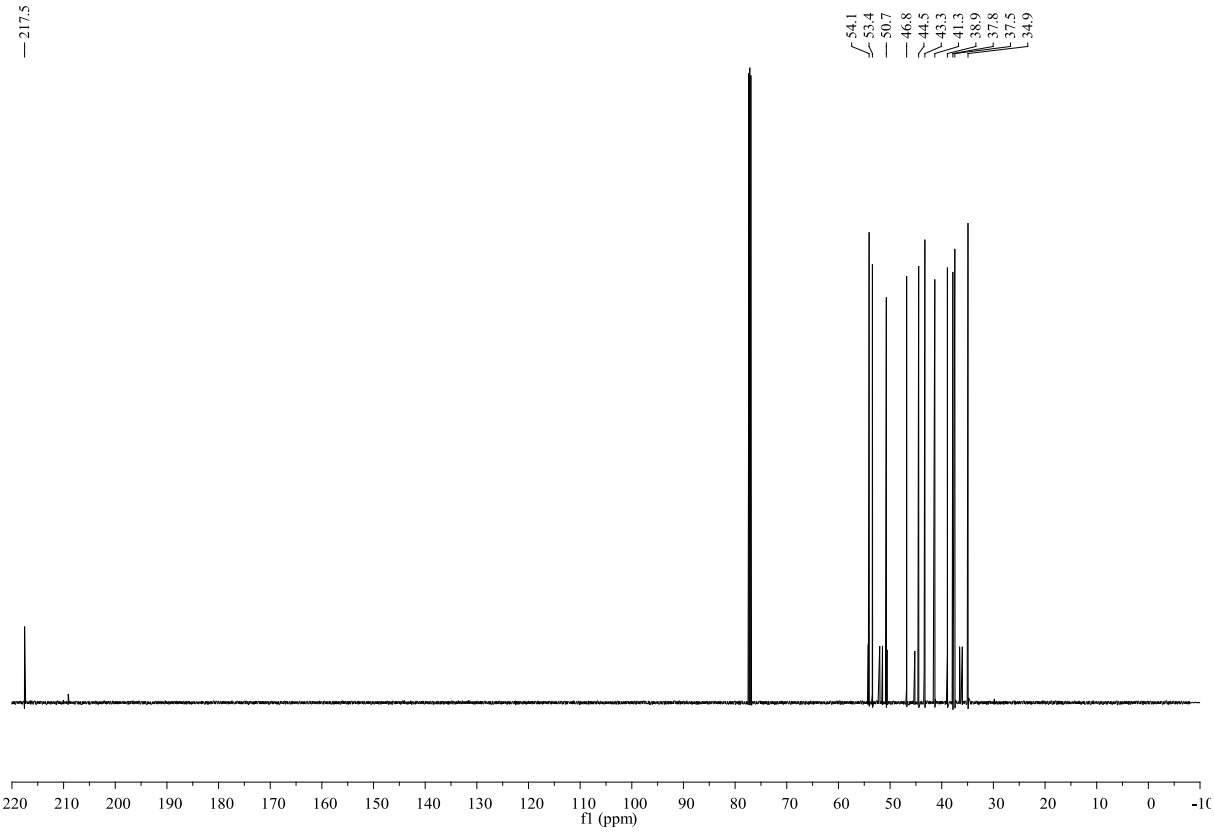


346 (^{1}H NMR, 600 MHz, $CDCl_3$)

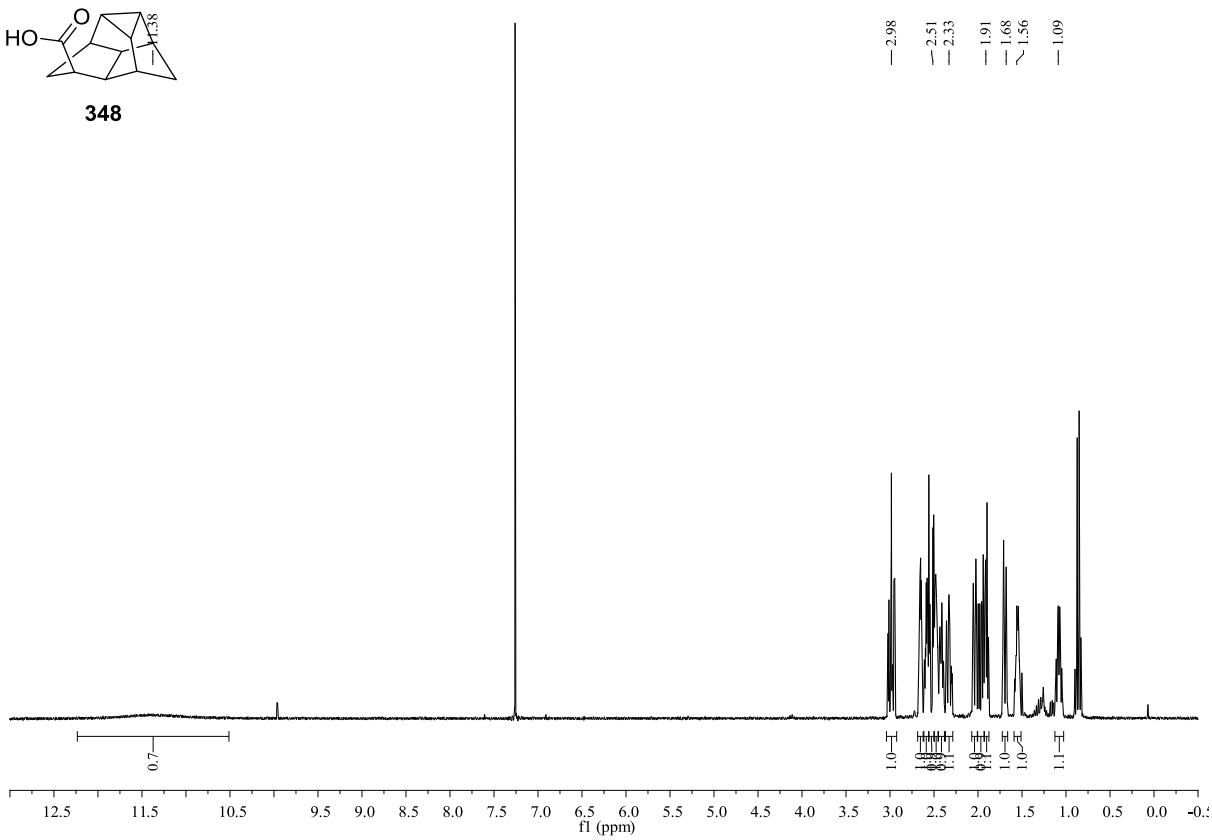


346

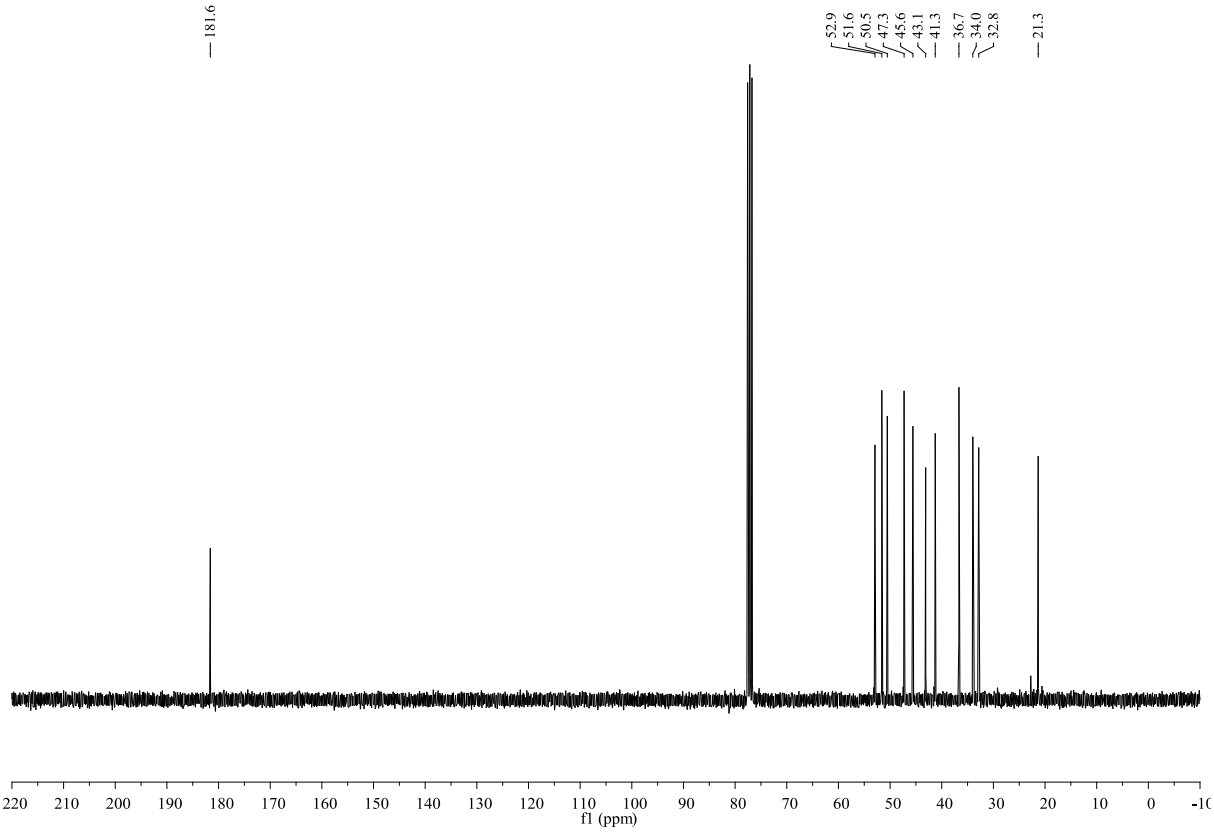
346 (^{13}C NMR, 150 MHz, $CDCl_3$)



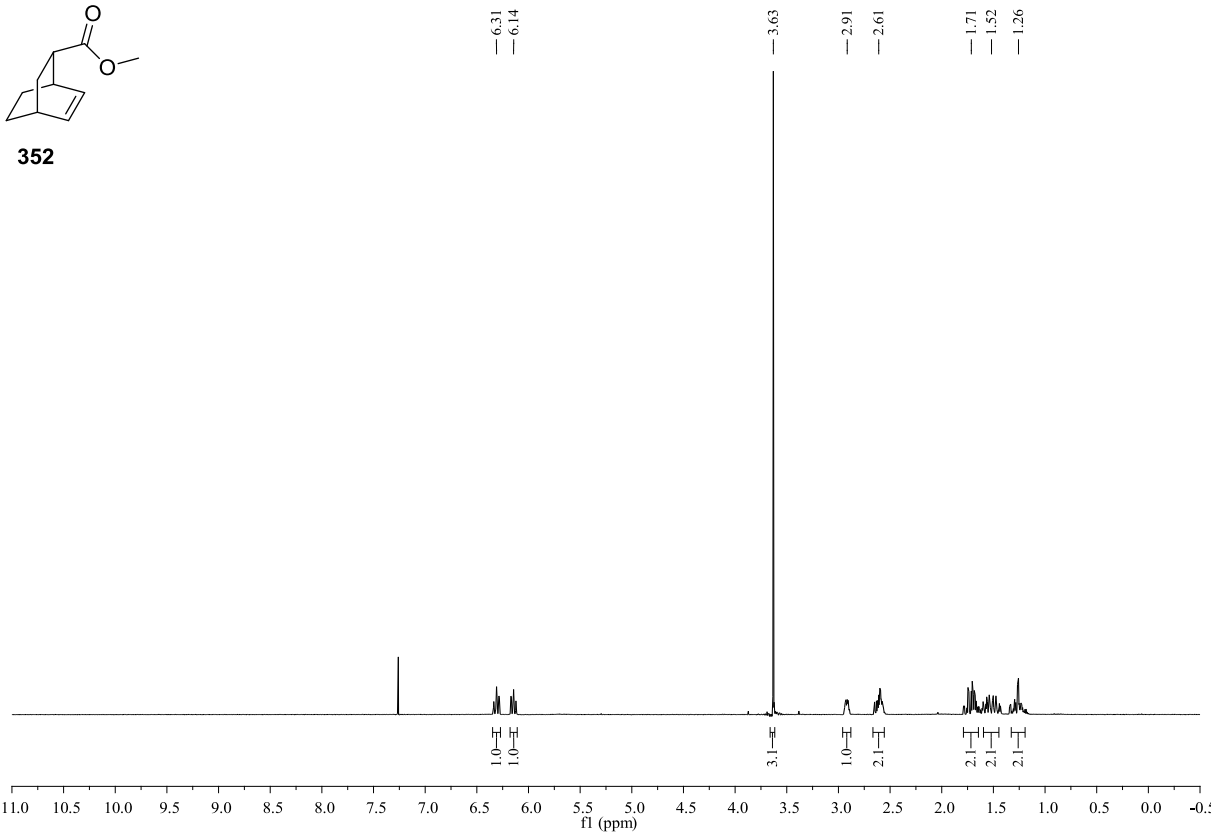
348 (^{1}H NMR, 300 MHz, $CDCl_3$)



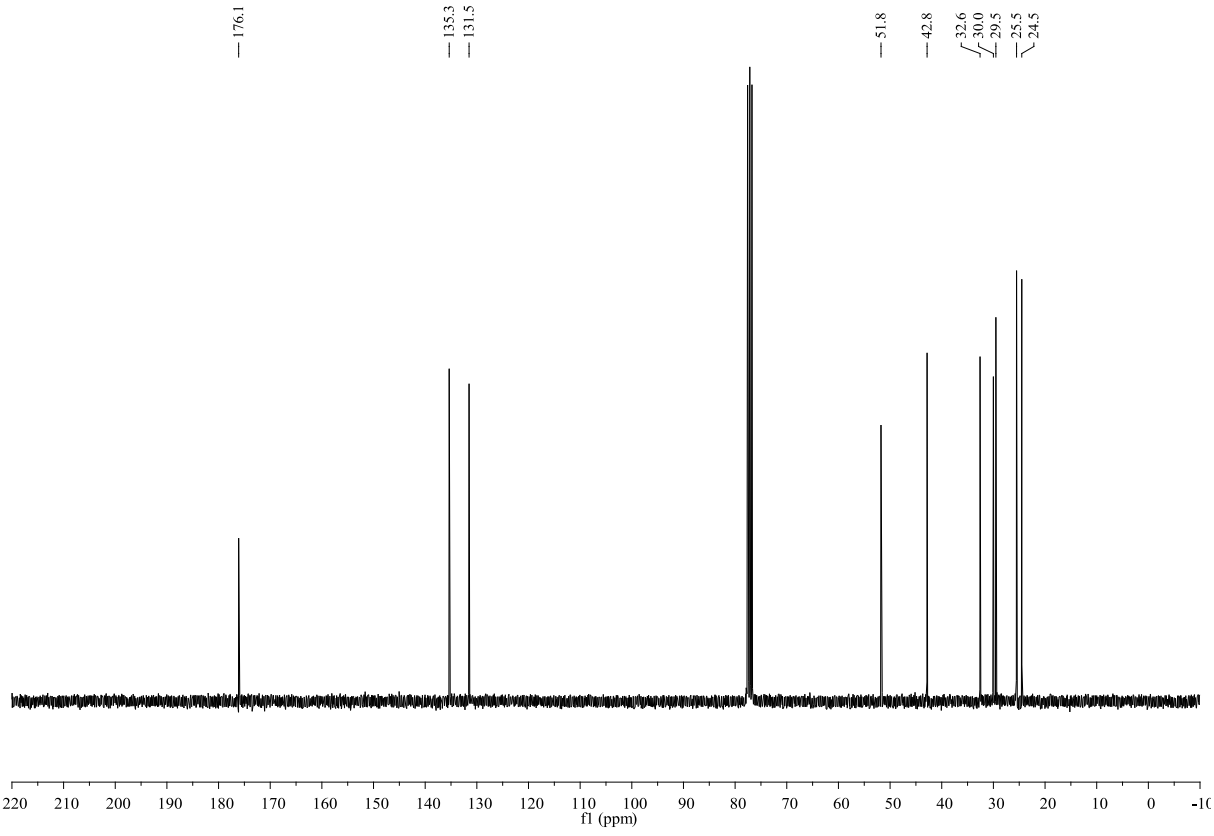
348 (^{13}C NMR, 75 MHz, $CDCl_3$)



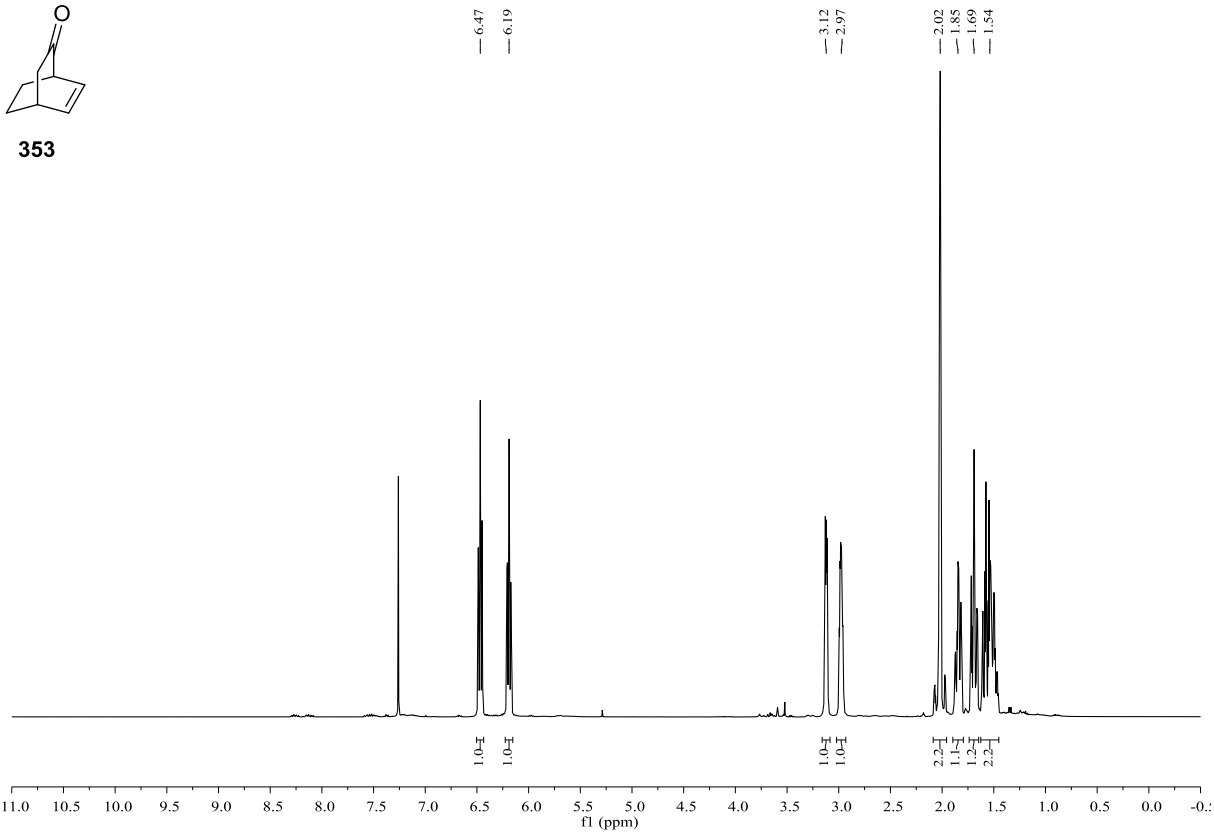
352 (^{1}H NMR, 300 MHz, $CDCl_3$)



352 (^{13}C NMR, 75 MHz, $CDCl_3$)

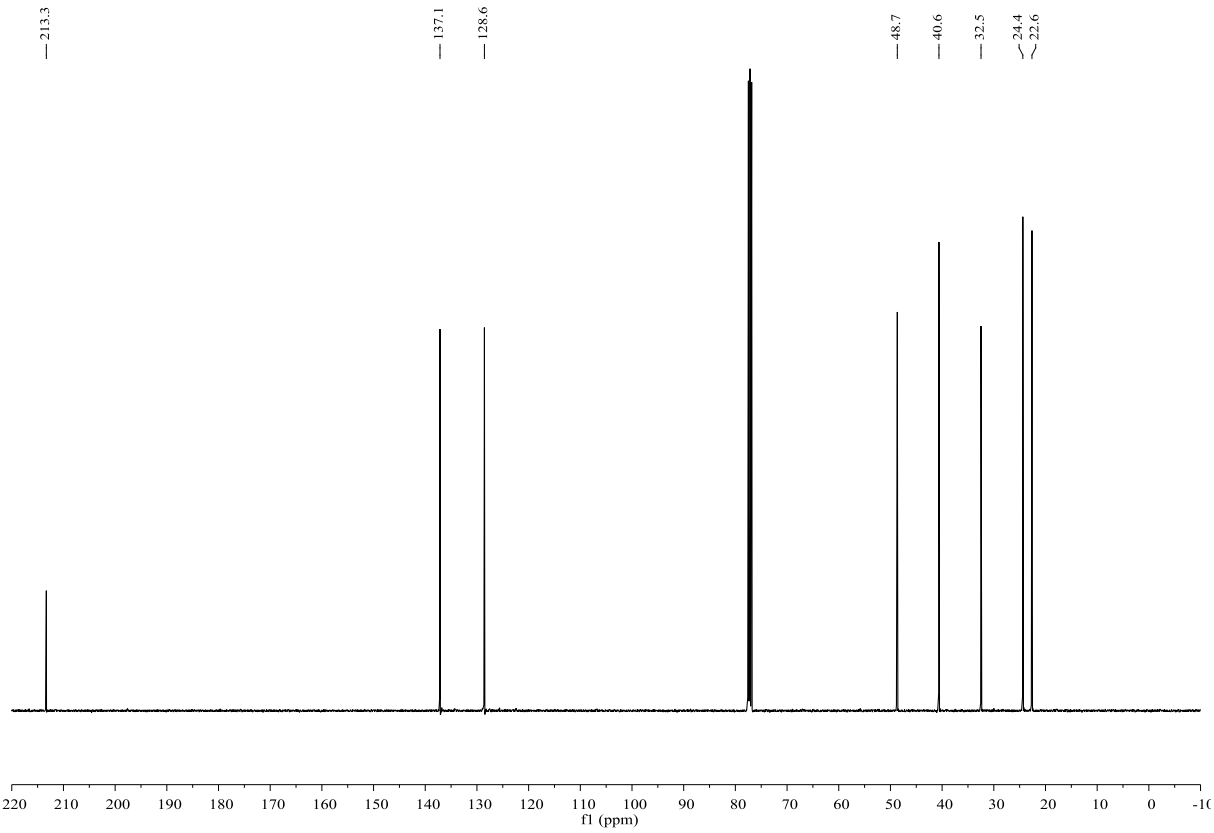


353 (^{1}H NMR, 400 MHz, $CDCl_3$)

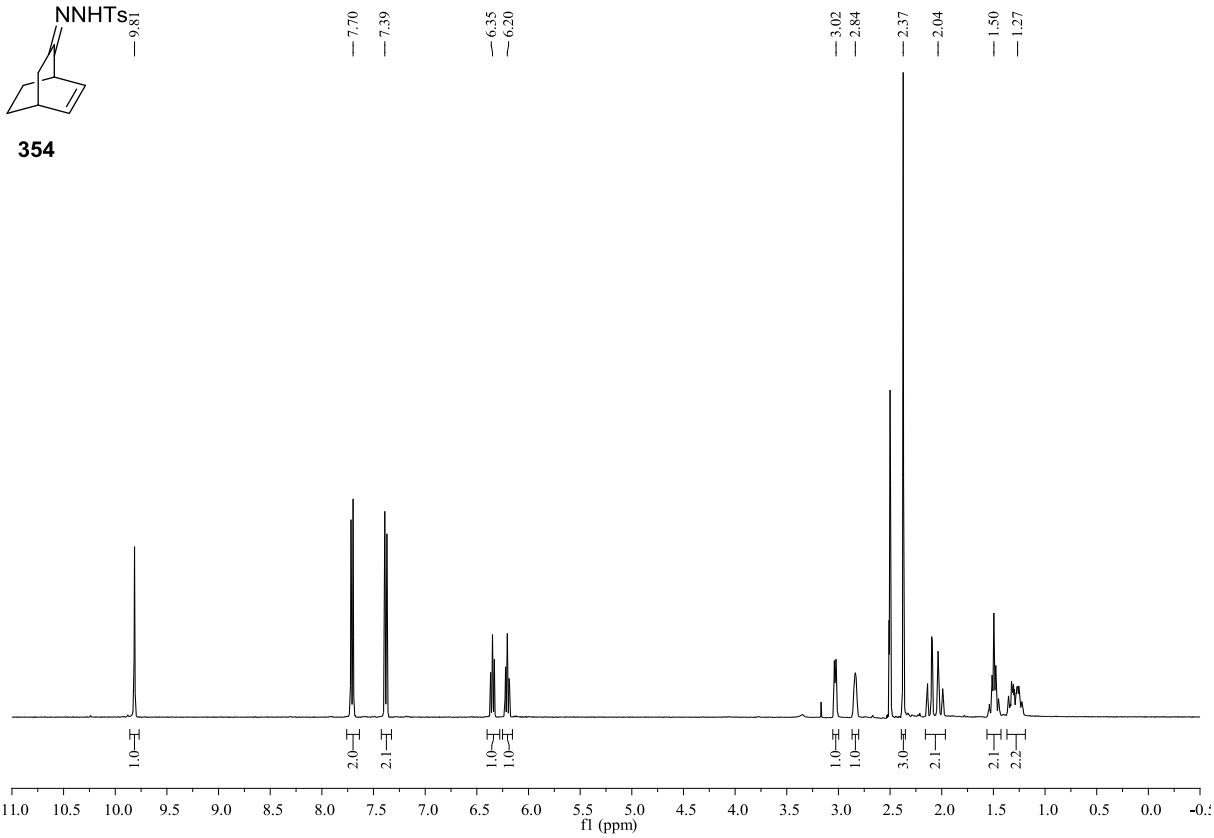


353

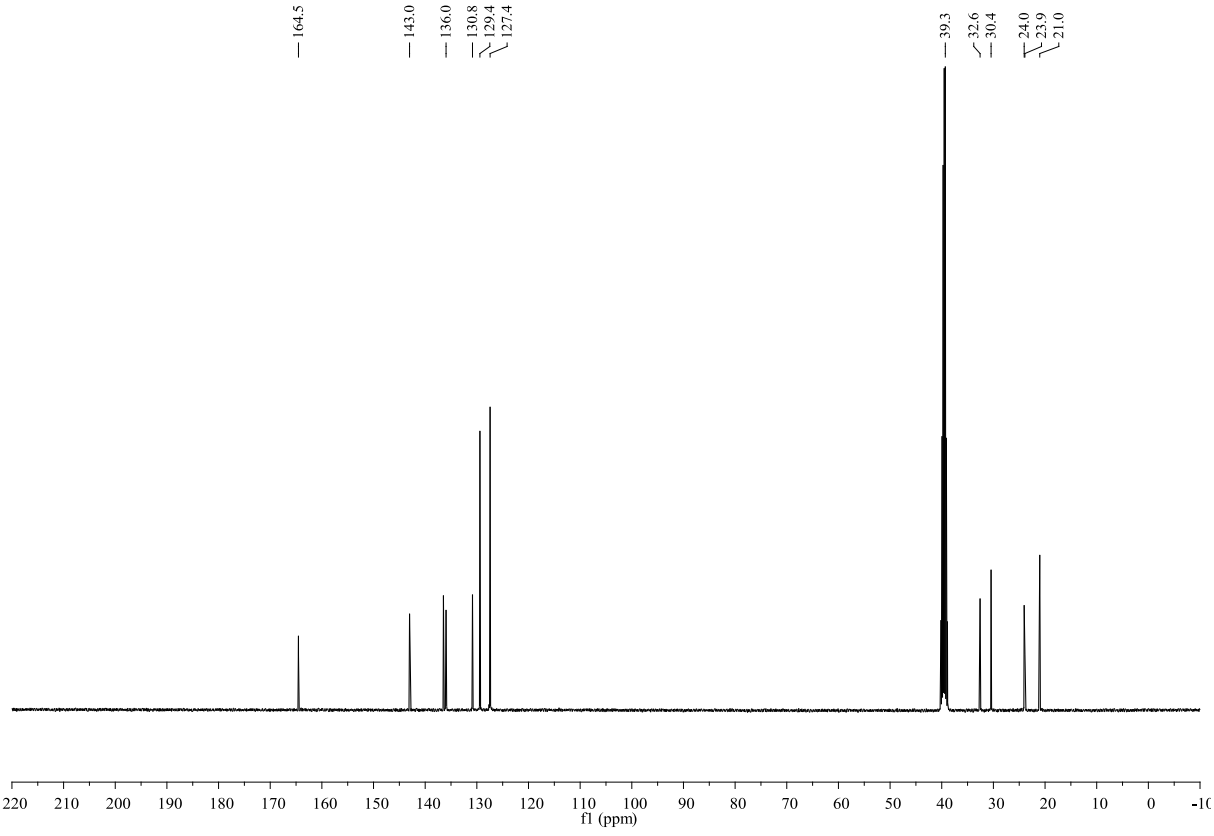
353 (^{13}C NMR, 100 MHz, $CDCl_3$)



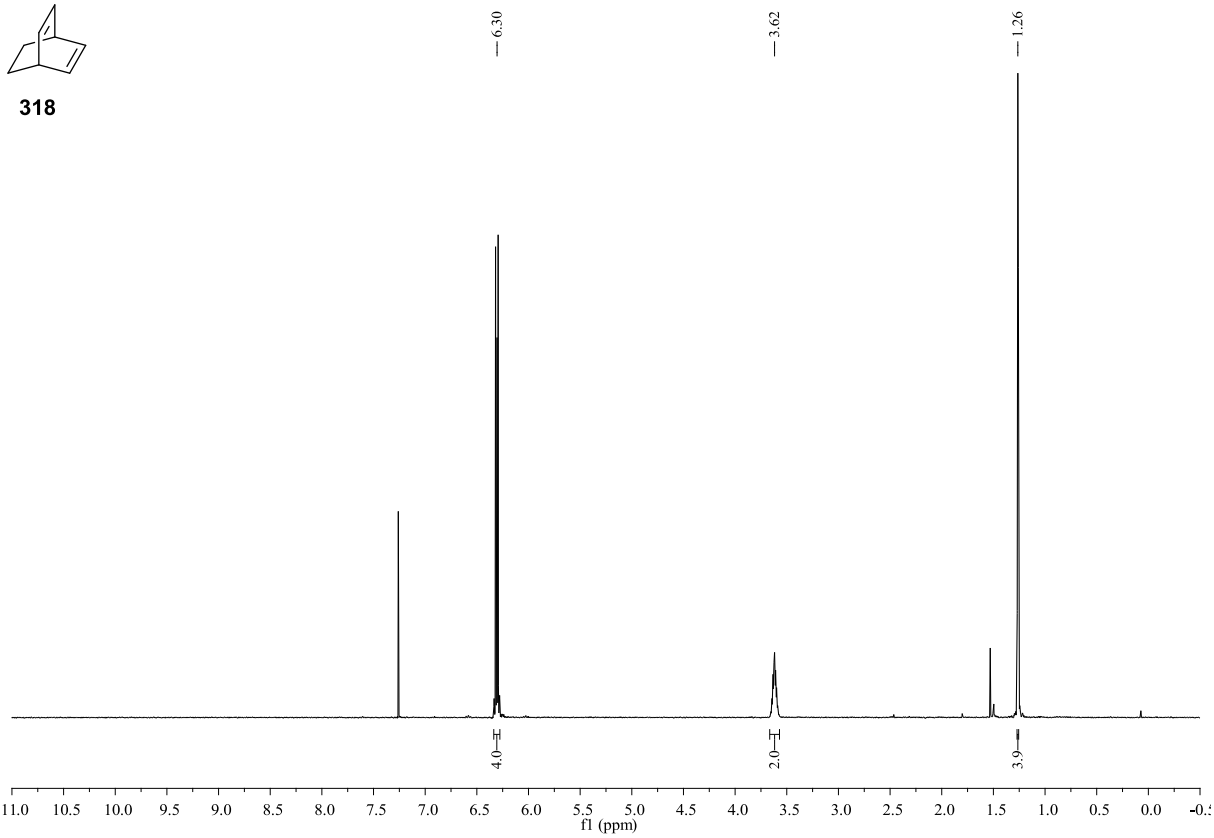
354 (^{1}H NMR, 400 MHz, DMSO-d_6)



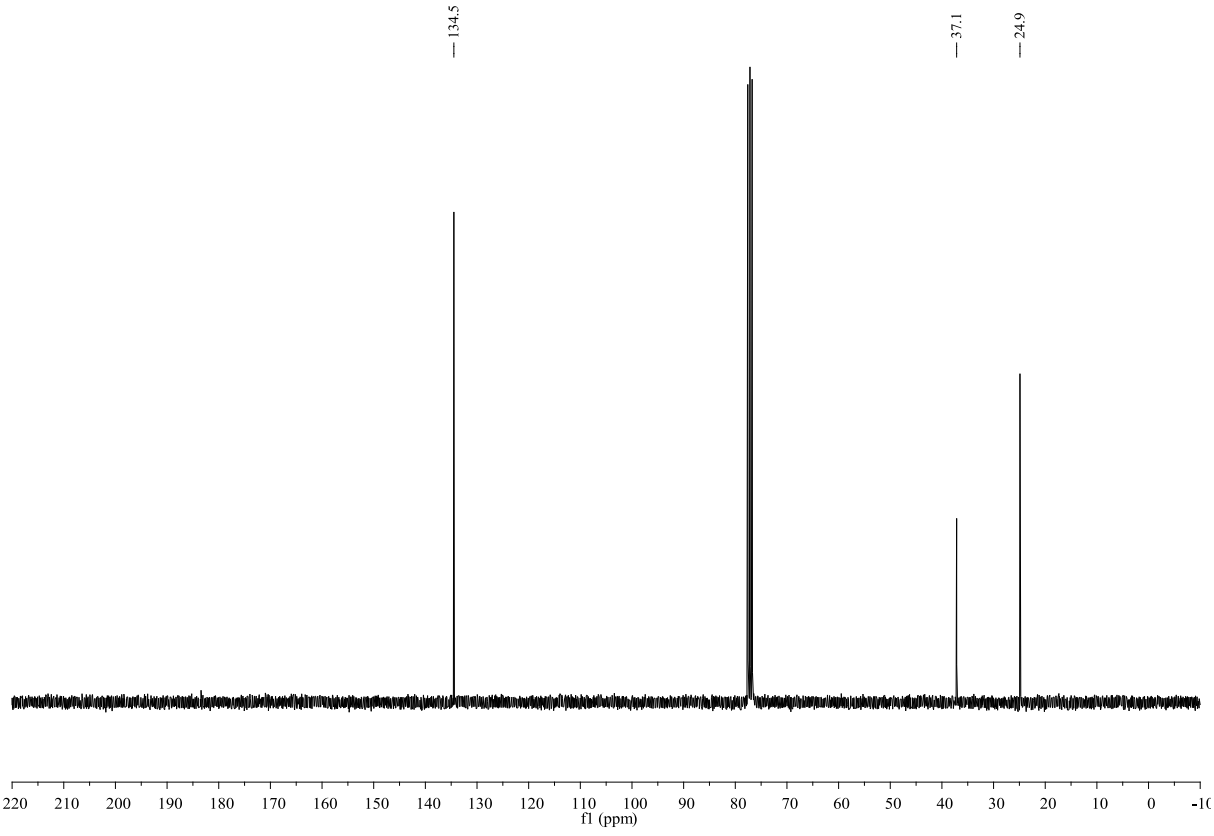
354 (^{13}C NMR, 100 MHz, DMSO-d_6)



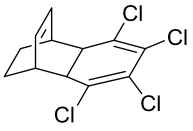
318 (^{1}H NMR, 300 MHz, $CDCl_3$)



318 (^{13}C NMR, 75 MHz, $CDCl_3$)

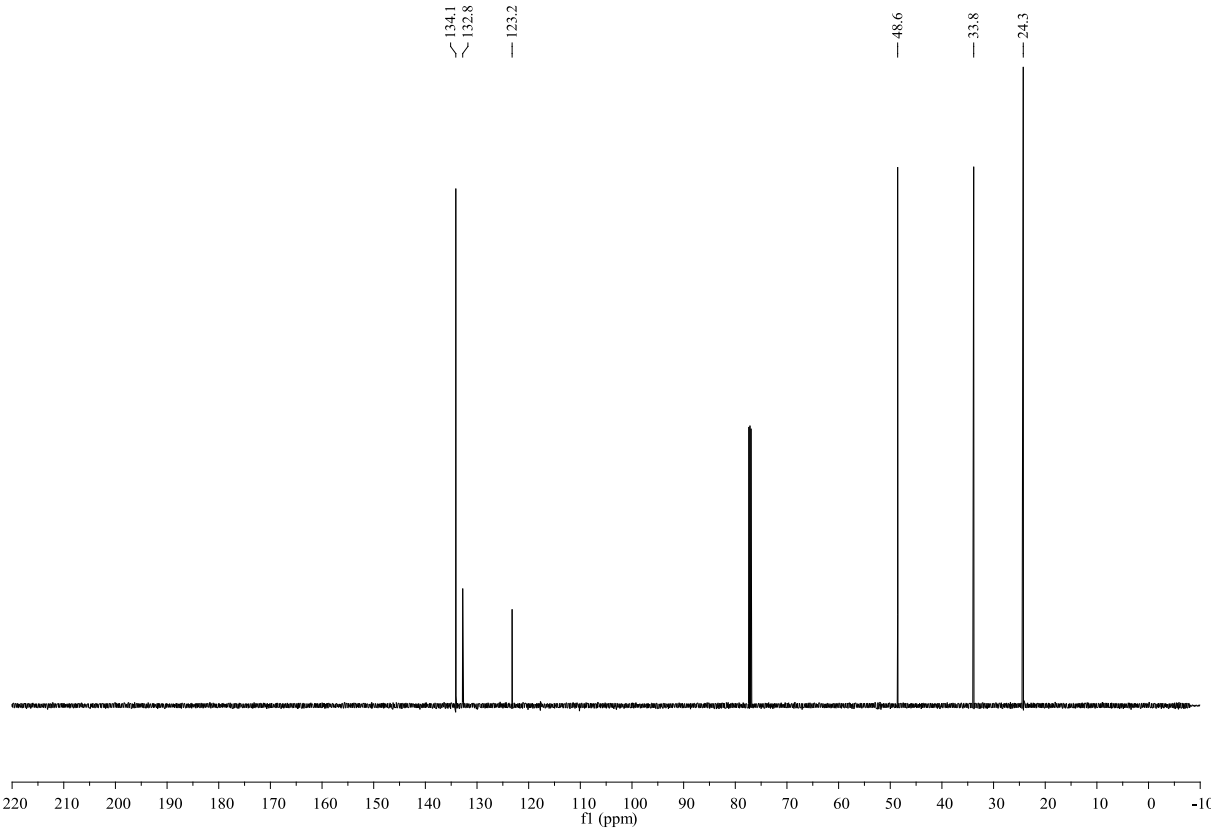


355 (^{1}H NMR, 600 MHz, $CDCl_3$)

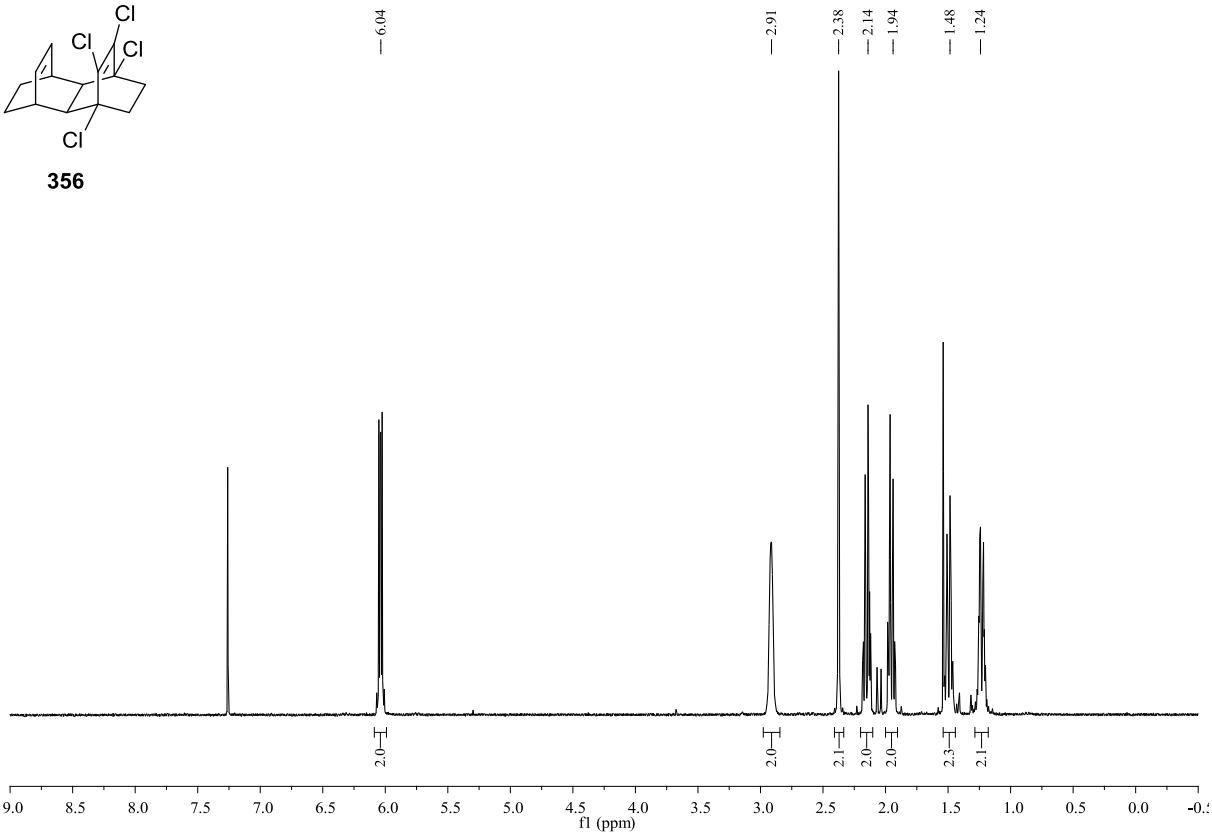


355

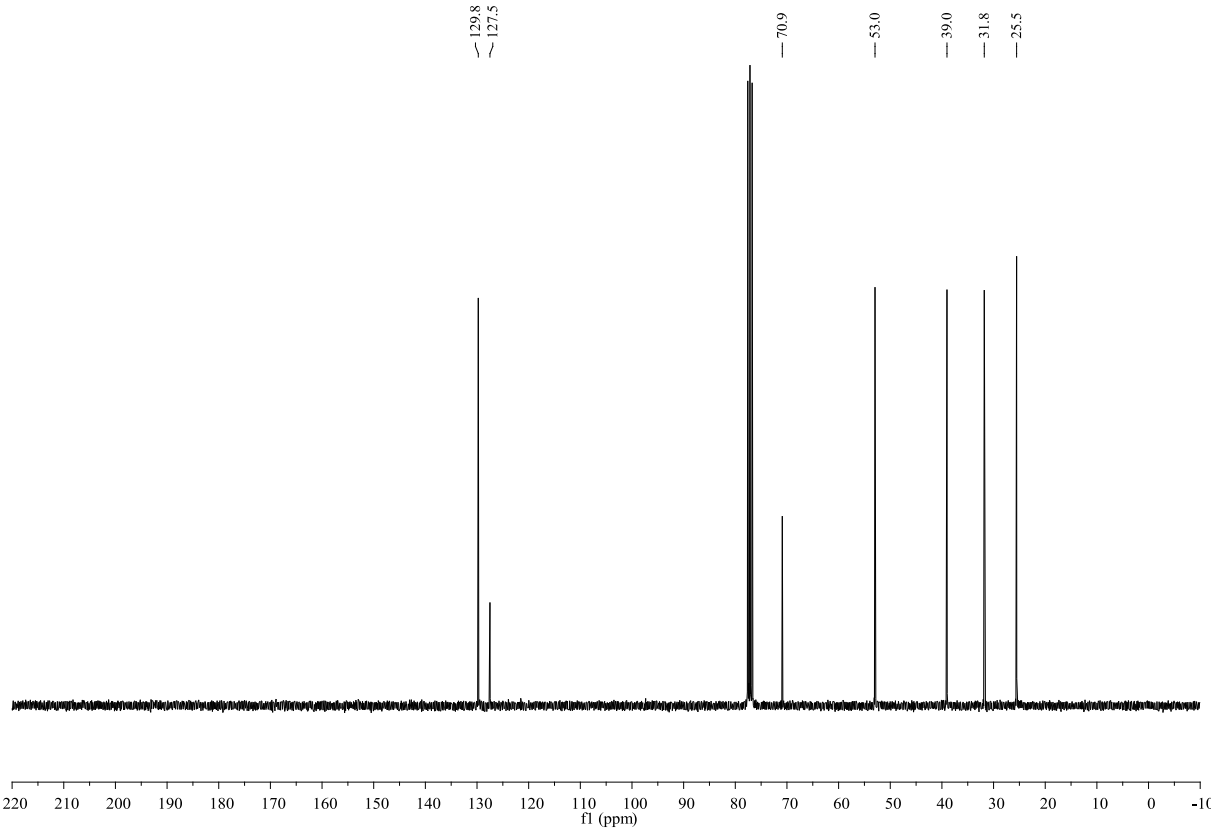
355 (^{13}C NMR, 150 MHz, $CDCl_3$)



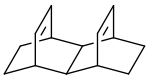
356 (^{1}H NMR, 300 MHz, $CDCl_3$)



356 (^{13}C NMR, 75 MHz, $CDCl_3$)

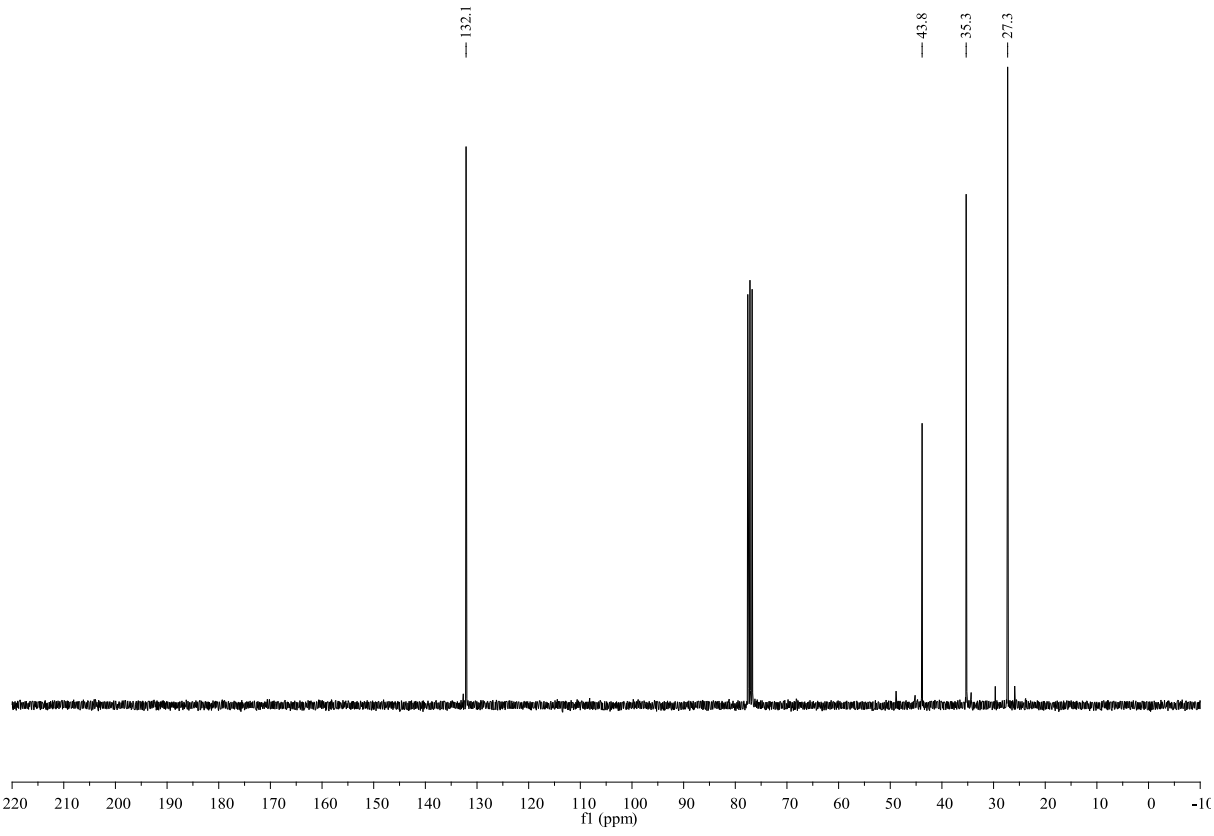


316 (^{1}H NMR, 300 MHz, $CDCl_3$)

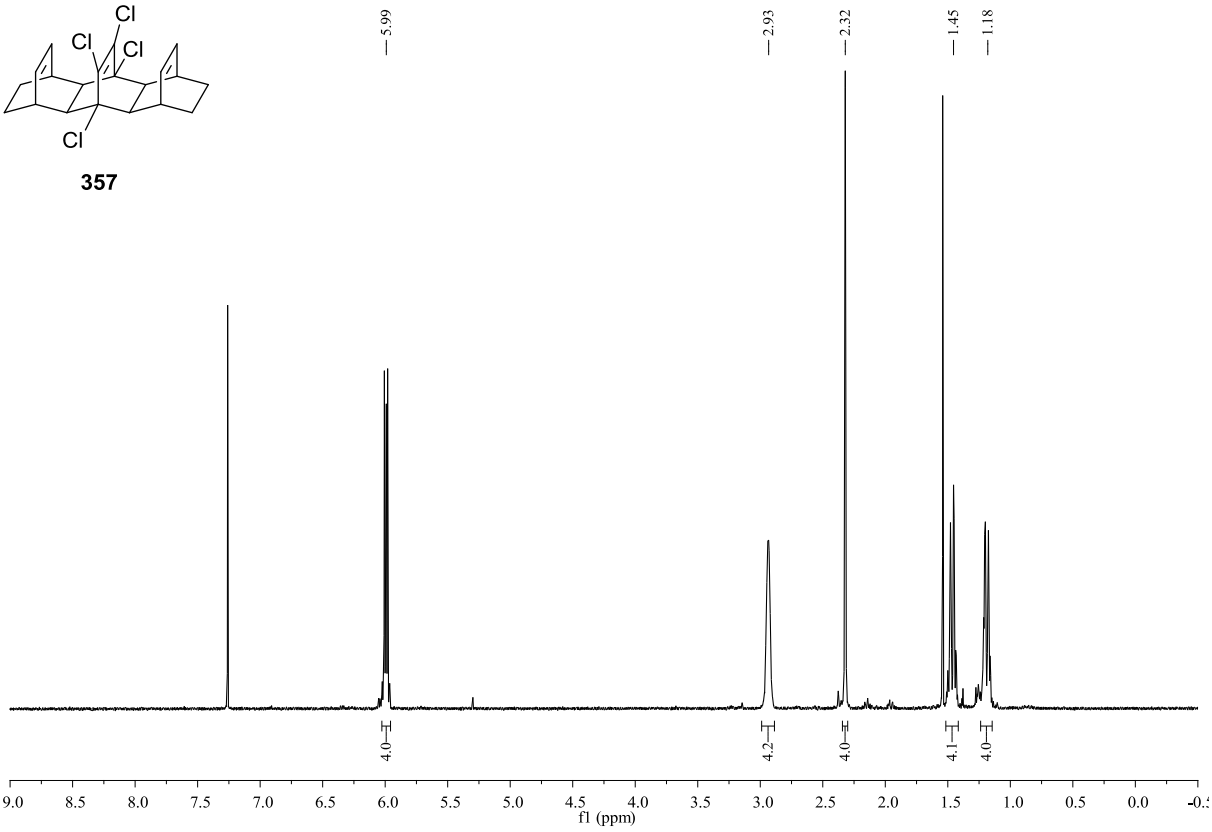


316

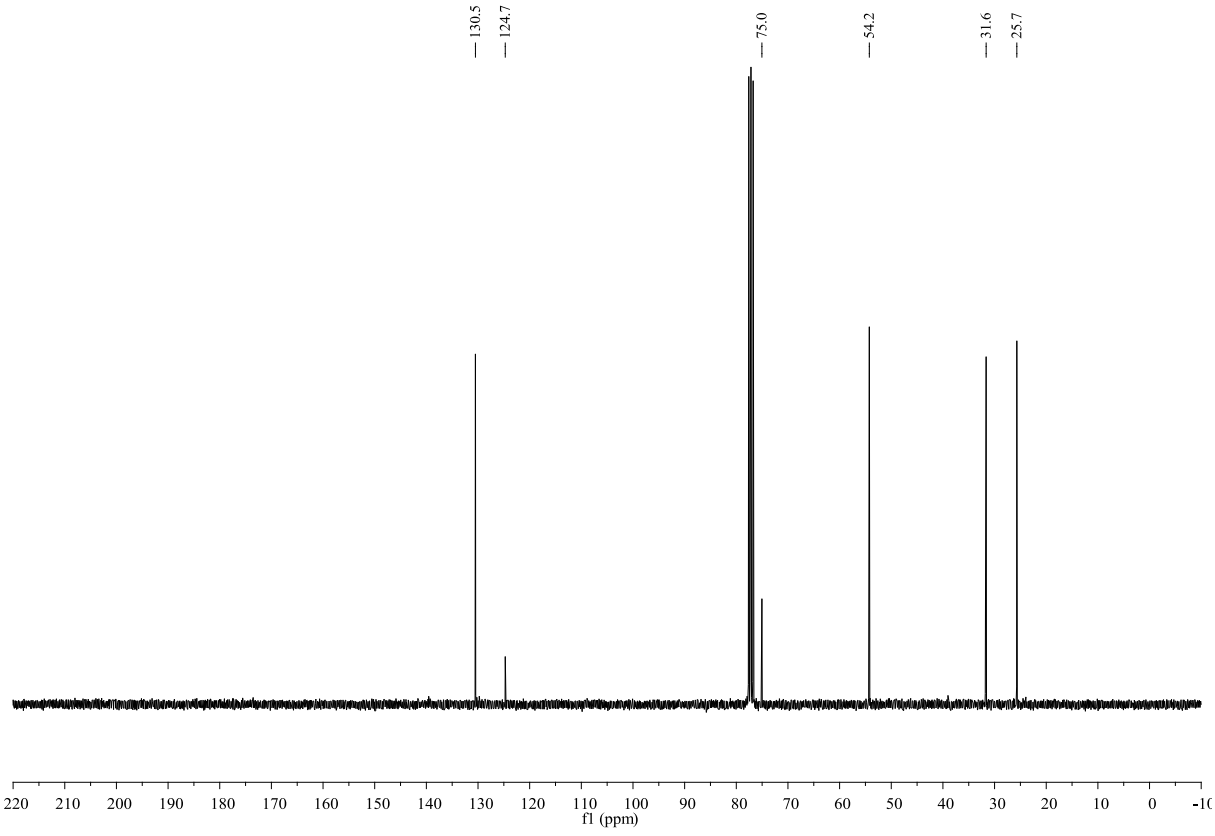
316 (^{13}C NMR, 75 MHz, $CDCl_3$)



357 (^{1}H NMR, 300 MHz, $CDCl_3$)



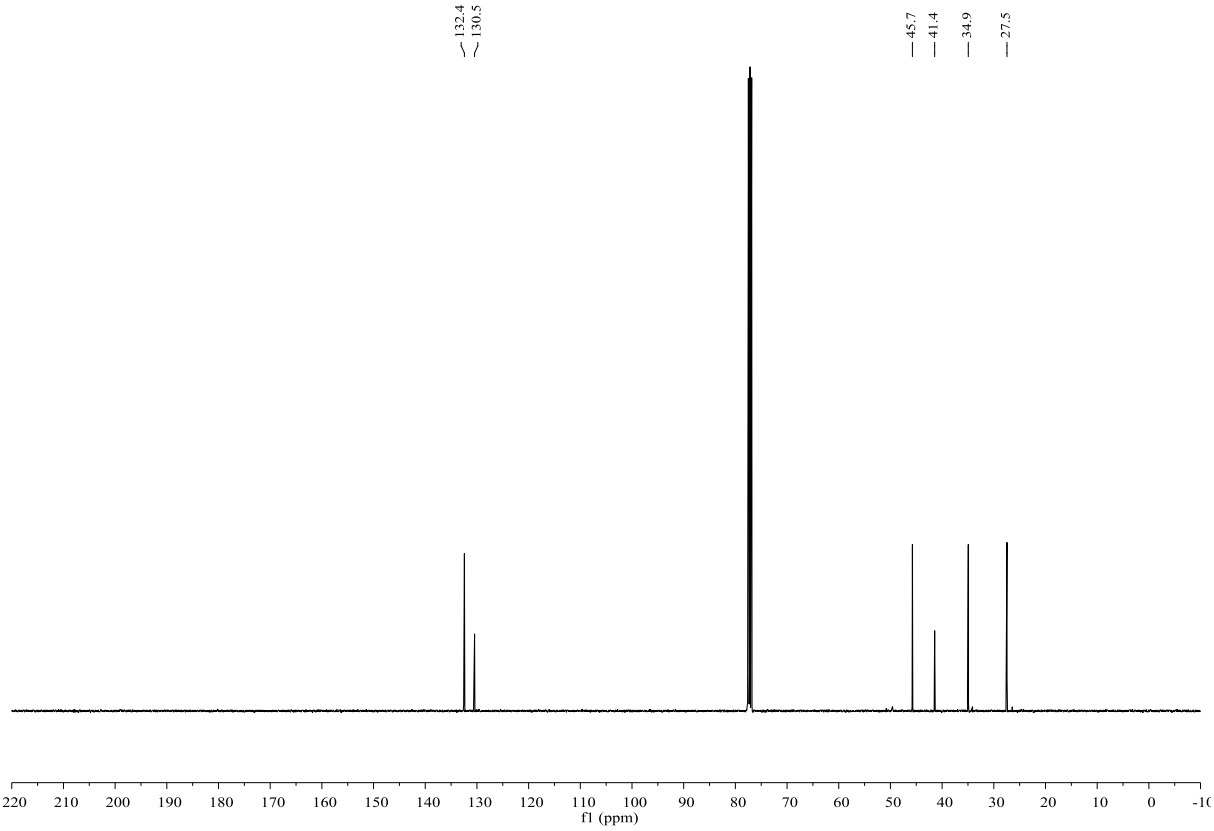
357 (^{13}C NMR, 75 MHz, $CDCl_3$)



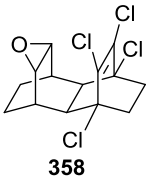
317 (^{1}H NMR, 400 MHz, $CDCl_3$)

317

317 (^{13}C NMR, 100 MHz, $CDCl_3$)

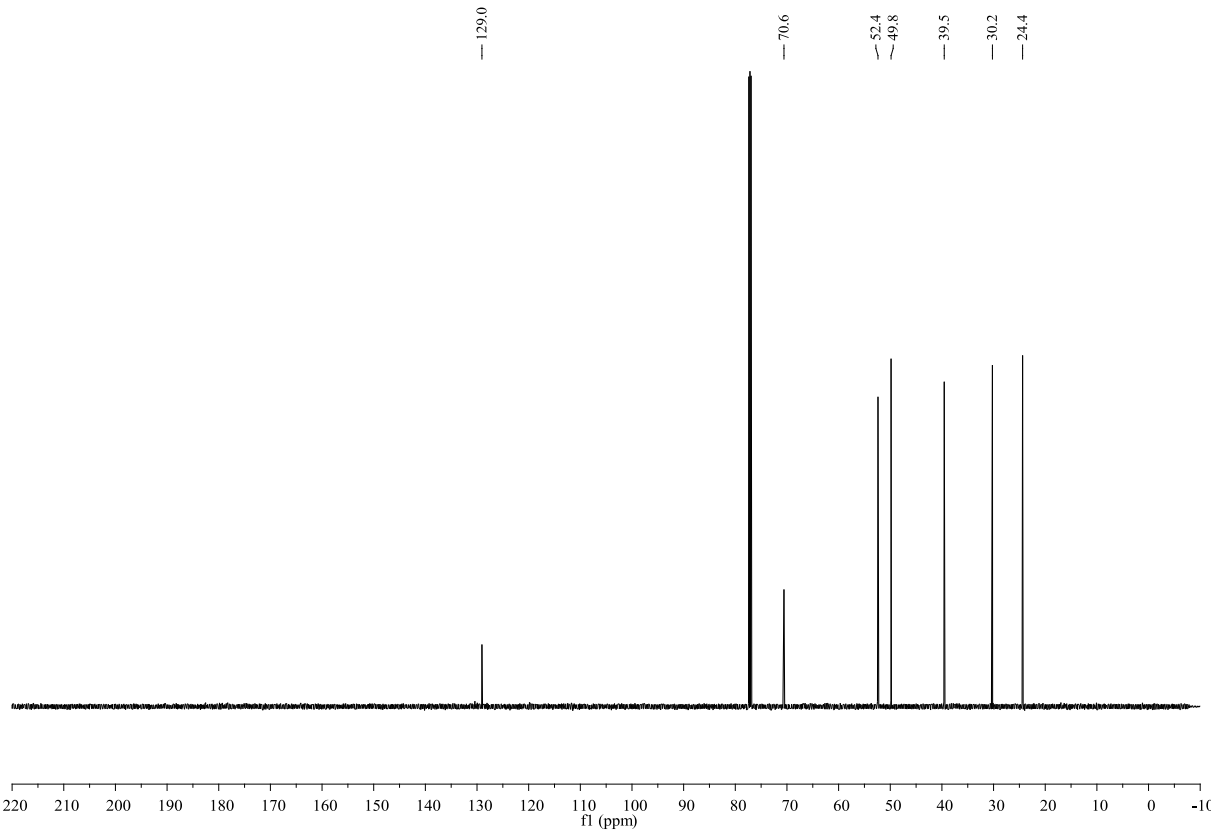


358 (^{1}H NMR, 600 MHz, $CDCl_3$)

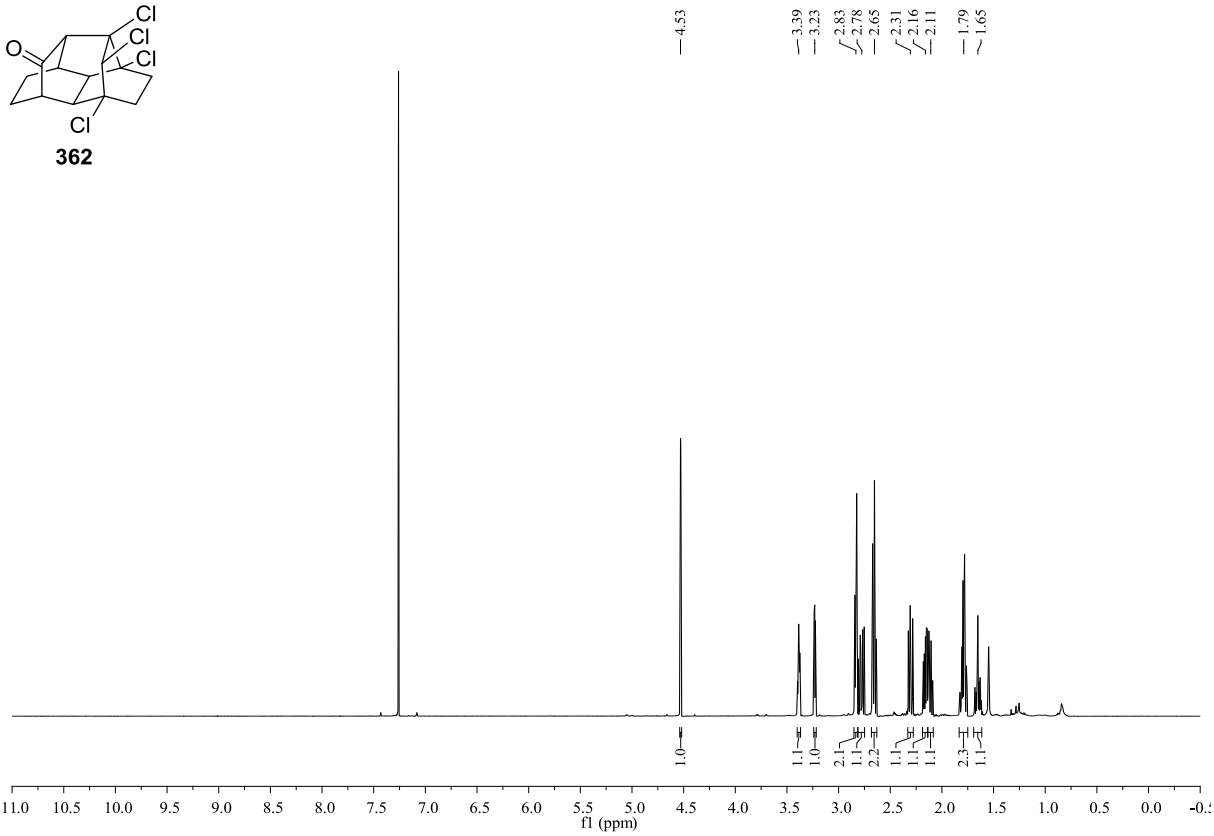


358

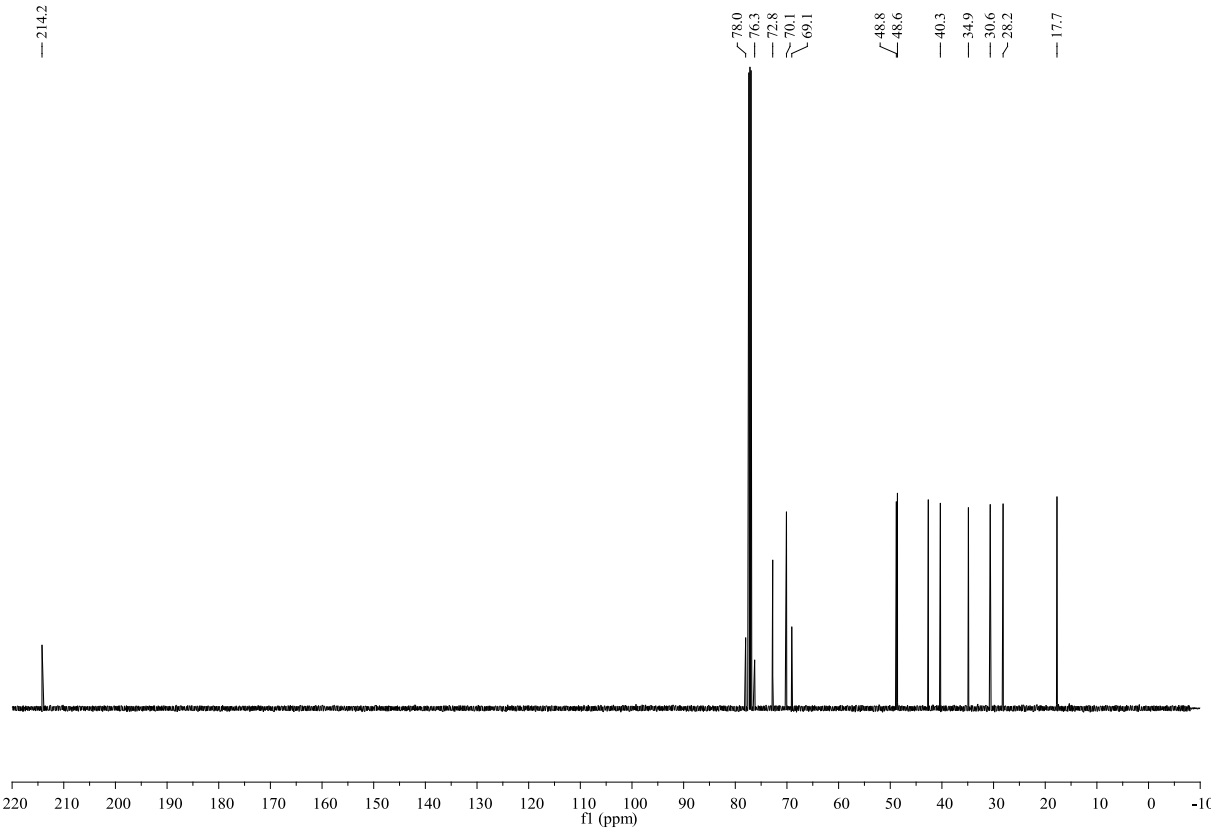
358 (^{13}C NMR, 150 MHz, $CDCl_3$)



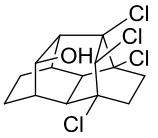
362 (^{1}H NMR, 600 MHz, $CDCl_3$)



362 (^{13}C NMR, 150 MHz, $CDCl_3$)

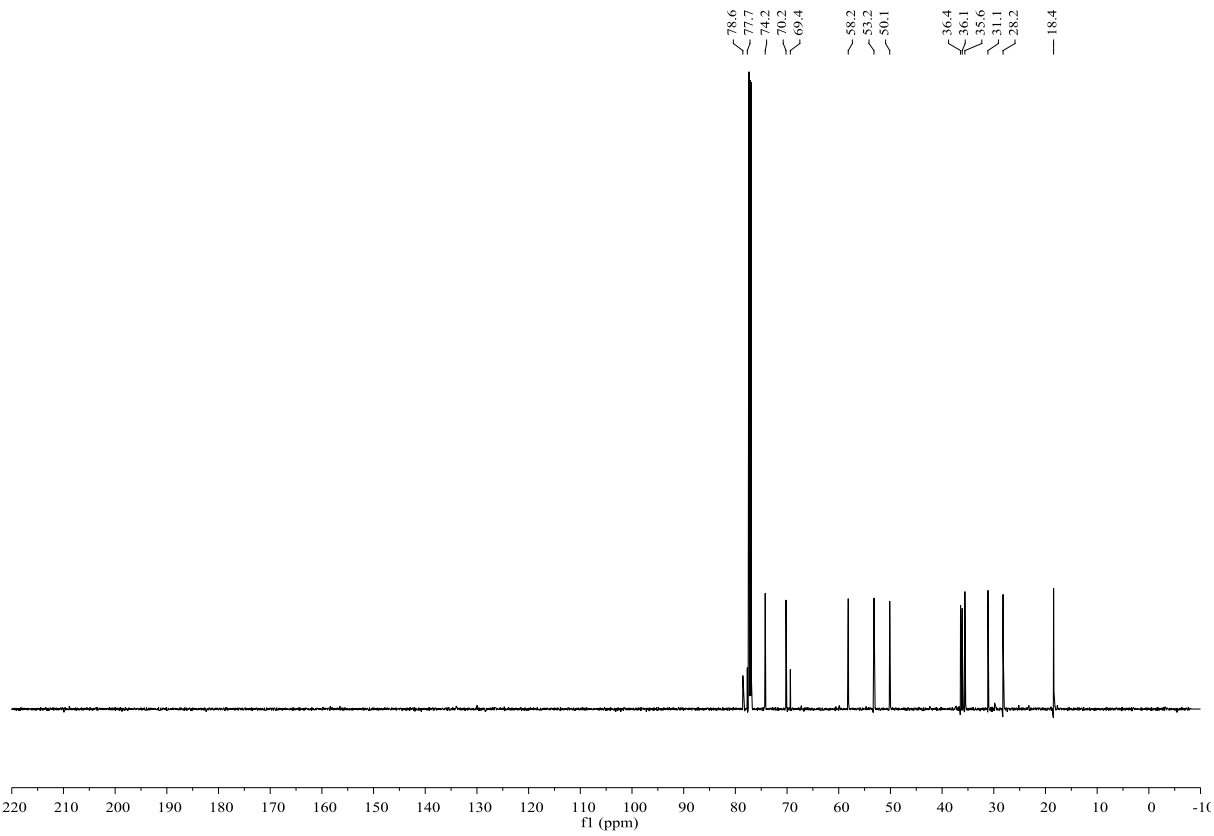


364 (^{1}H NMR, 600 MHz, $CDCl_3$)

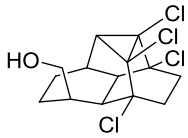


364

364 (^{13}C NMR, 150 MHz, $CDCl_3$)

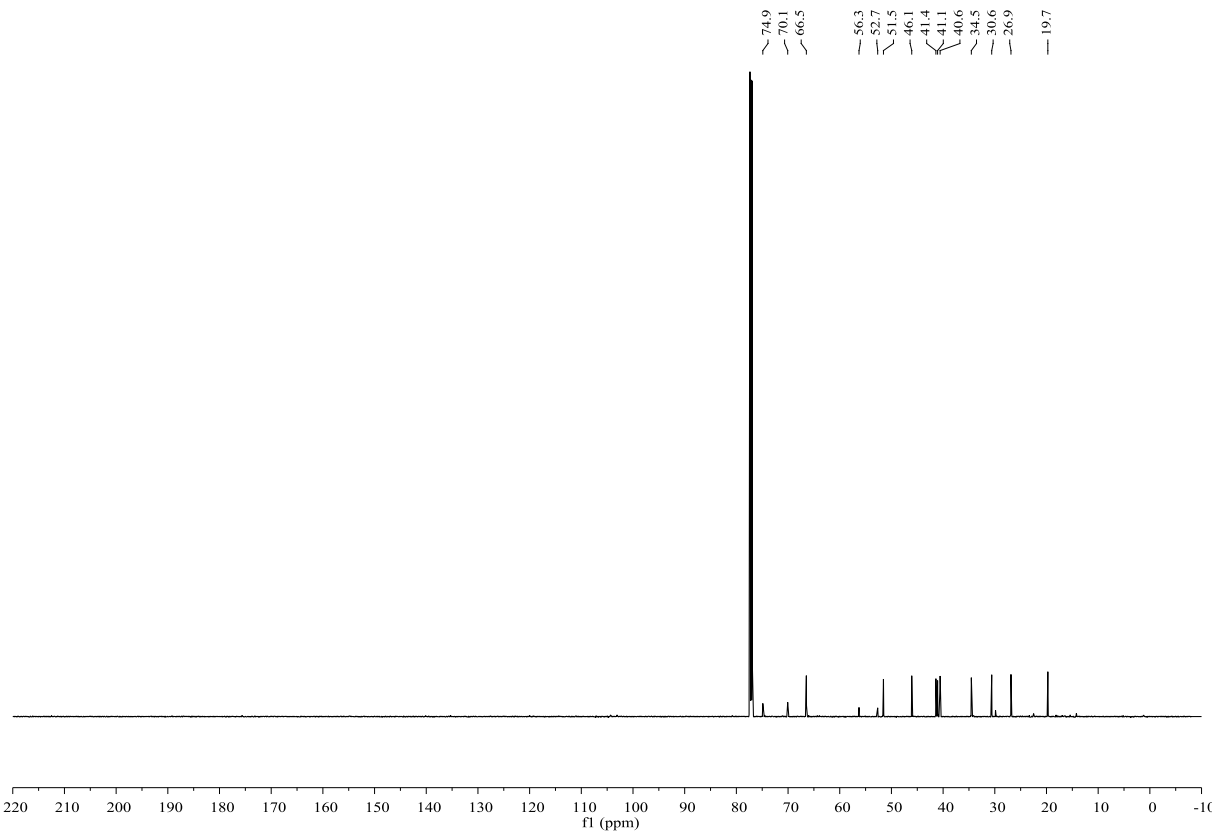


366 (^{1}H NMR, 600 MHz, $CDCl_3$)

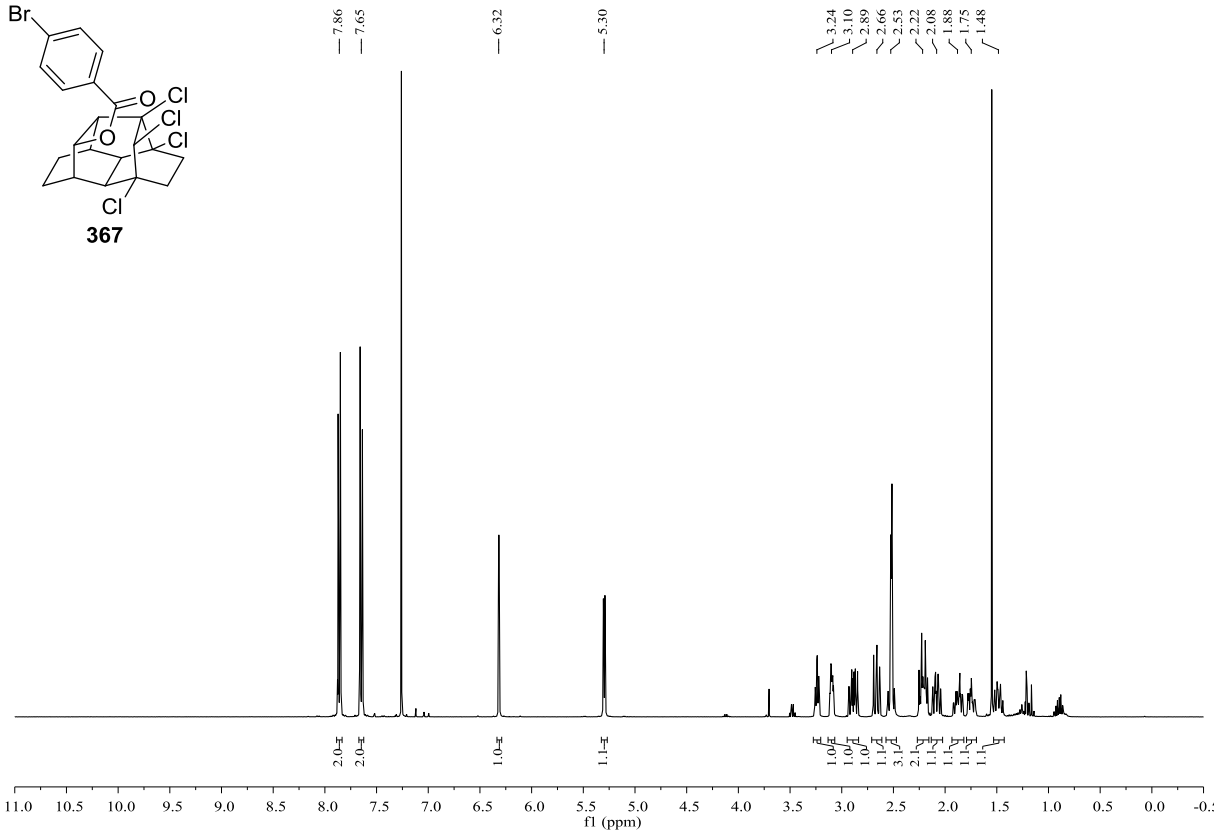


366

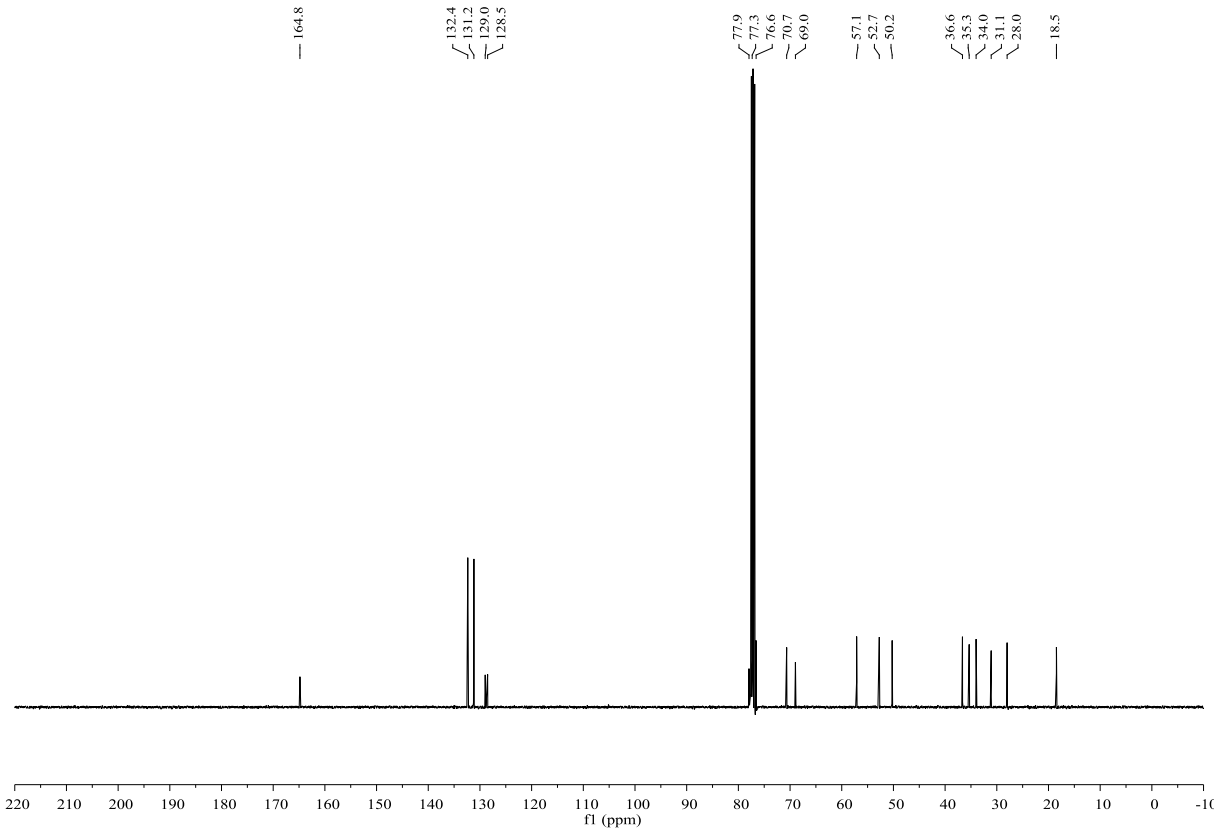
366 (^{13}C NMR, 150 MHz, $CDCl_3$)



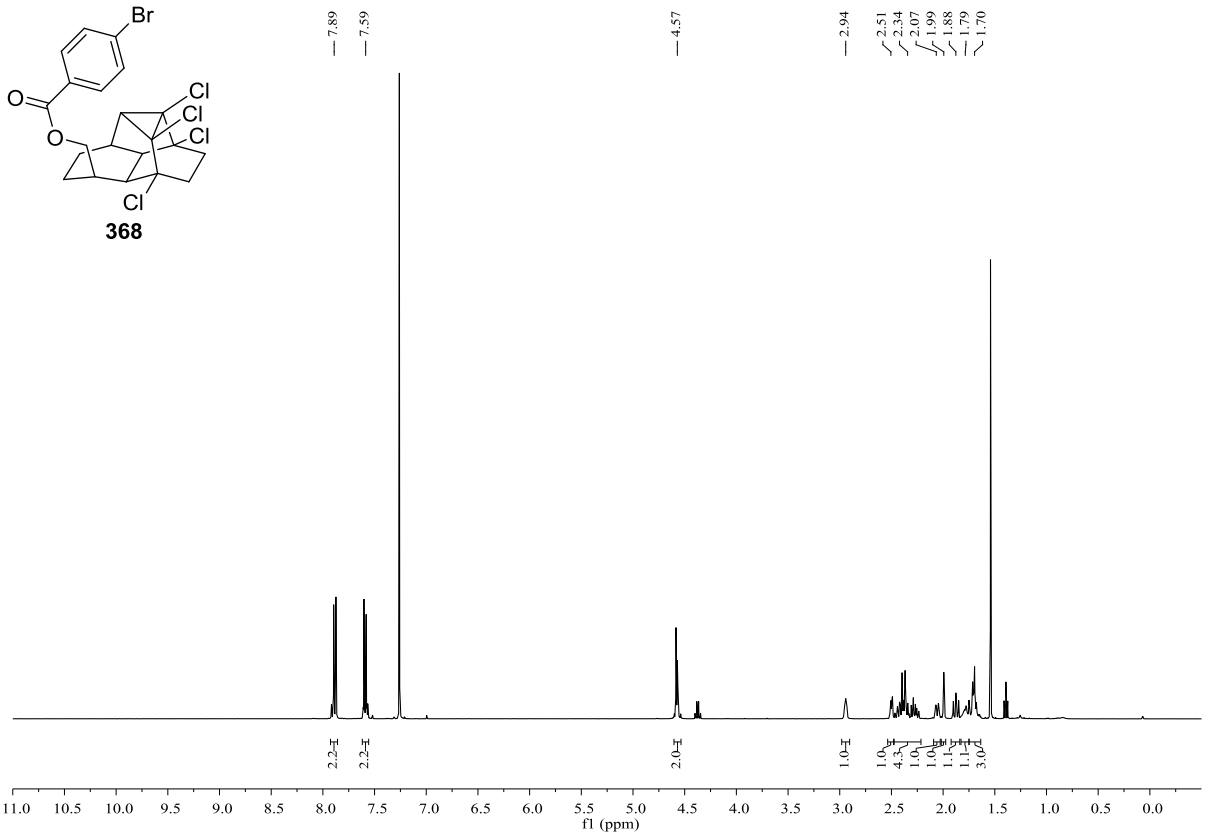
367 (^{1}H NMR, 400 MHz, $CDCl_3$)



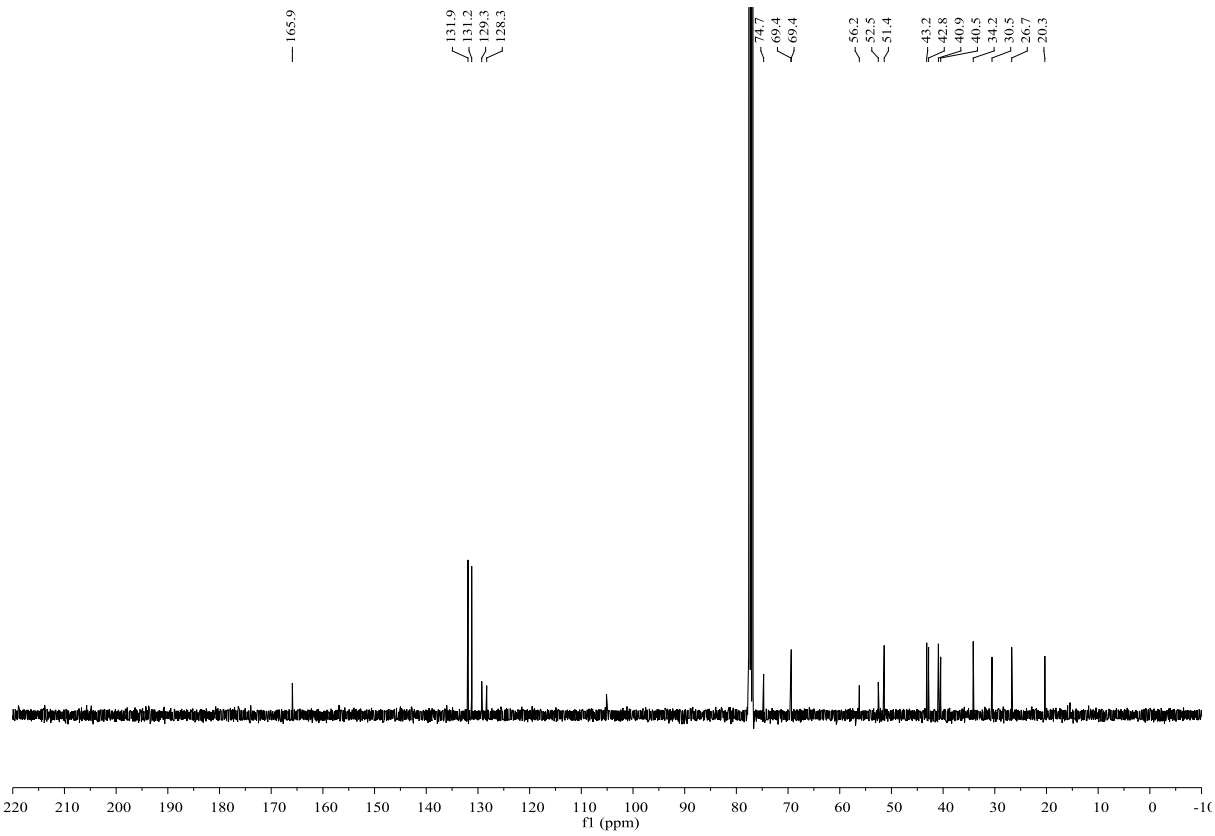
367 (^{13}C NMR, 100 MHz, $CDCl_3$)



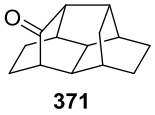
368 (^{1}H NMR, 400 MHz, $CDCl_3$)



368 (^{13}C NMR, 100 MHz, $CDCl_3$)

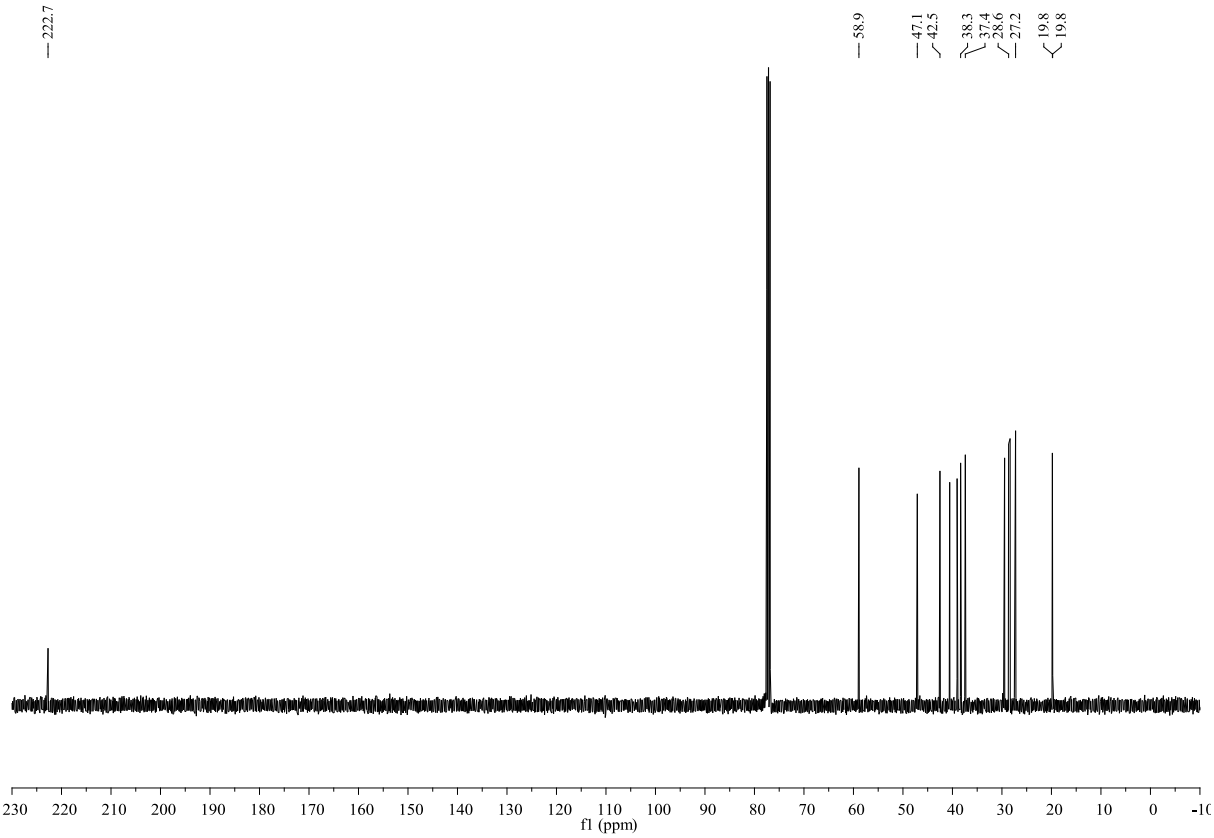


371 (^{1}H NMR, 300 MHz, $CDCl_3$)

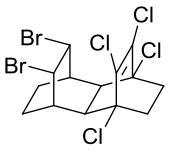


371

371 (^{13}C NMR, 100 MHz, $CDCl_3$)

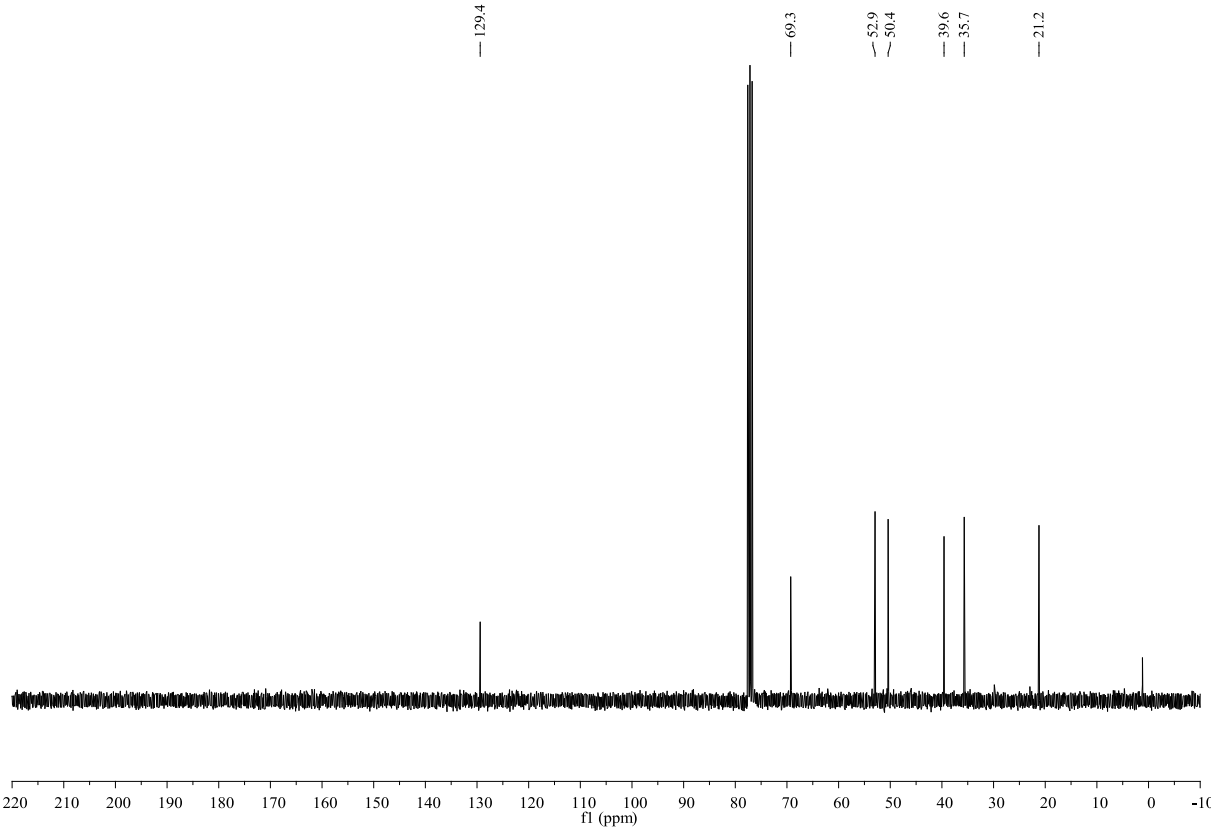


374 (^{1}H NMR, 300 MHz, $CDCl_3$)

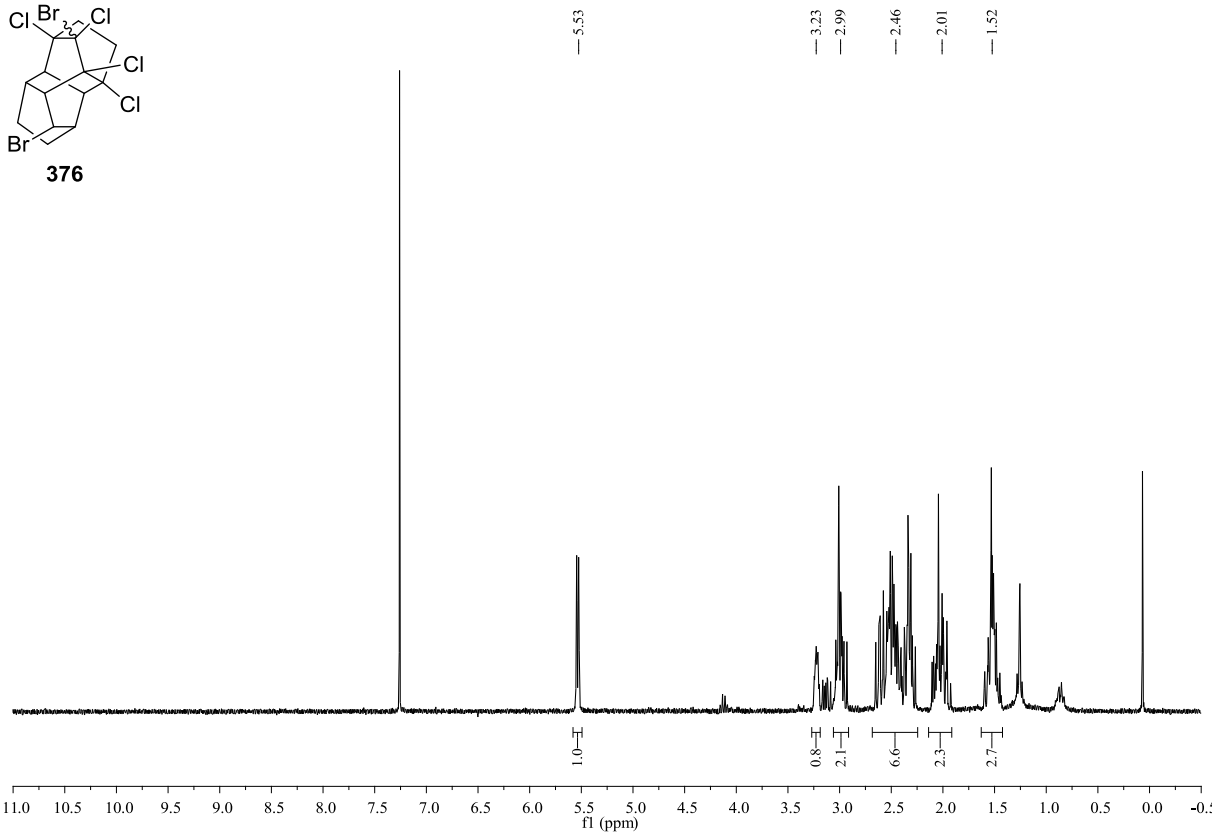


374

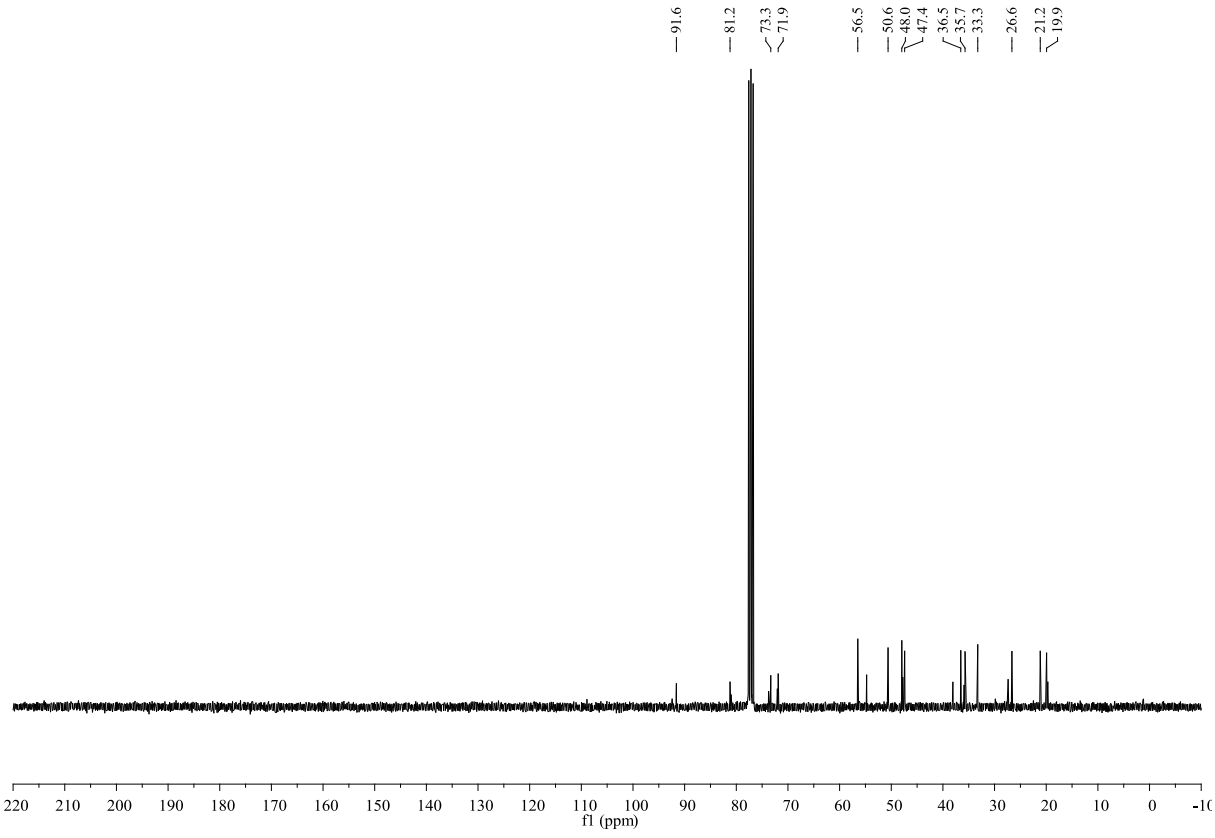
374 (^{13}C NMR, 75 MHz, $CDCl_3$)



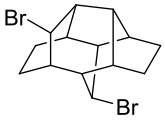
376 (^{1}H NMR, 300 MHz, $CDCl_3$)



376 (^{13}C NMR, 75 MHz, $CDCl_3$)

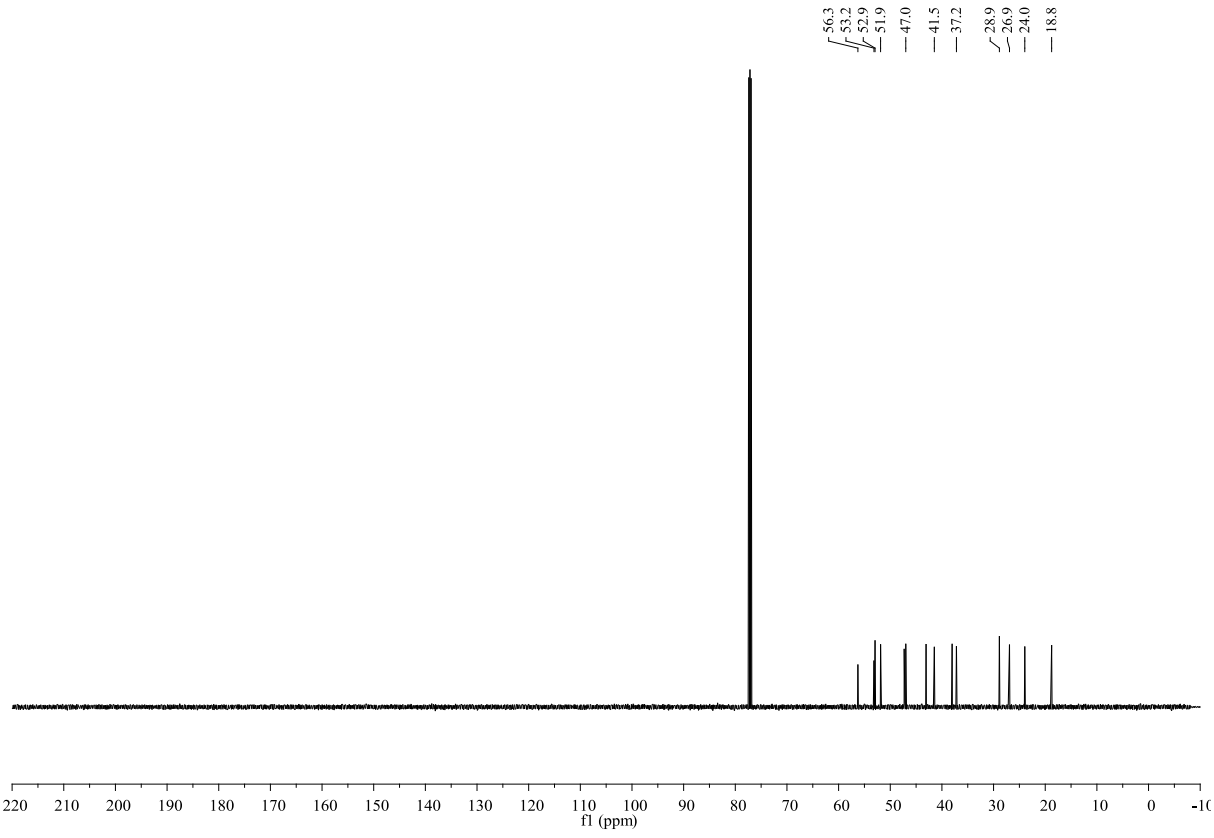


380 (^{1}H NMR, 600 MHz, $CDCl_3$)

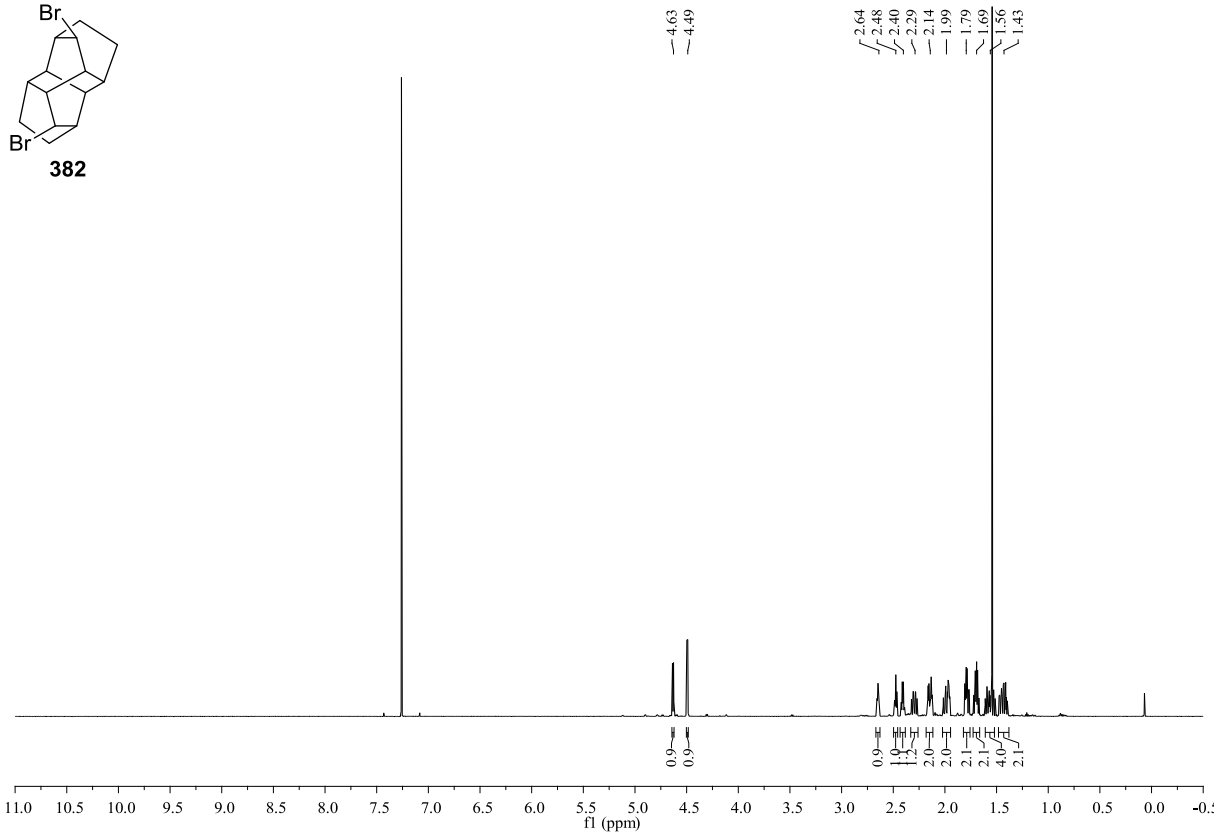


380

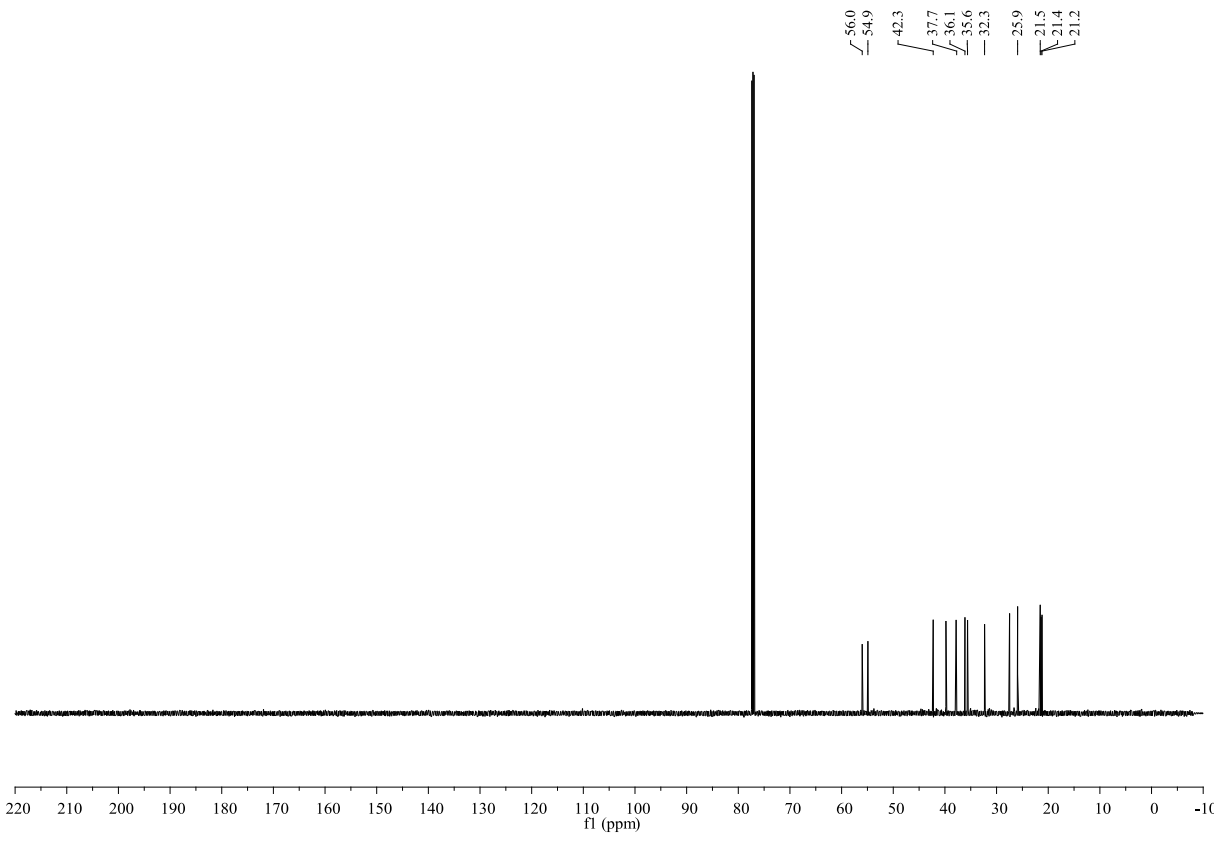
380 (^{13}C NMR, 150 MHz, $CDCl_3$)



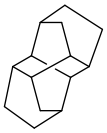
382 (^{1}H NMR, 600 MHz, $CDCl_3$)



382 (^{13}C NMR, 150 MHz, $CDCl_3$)

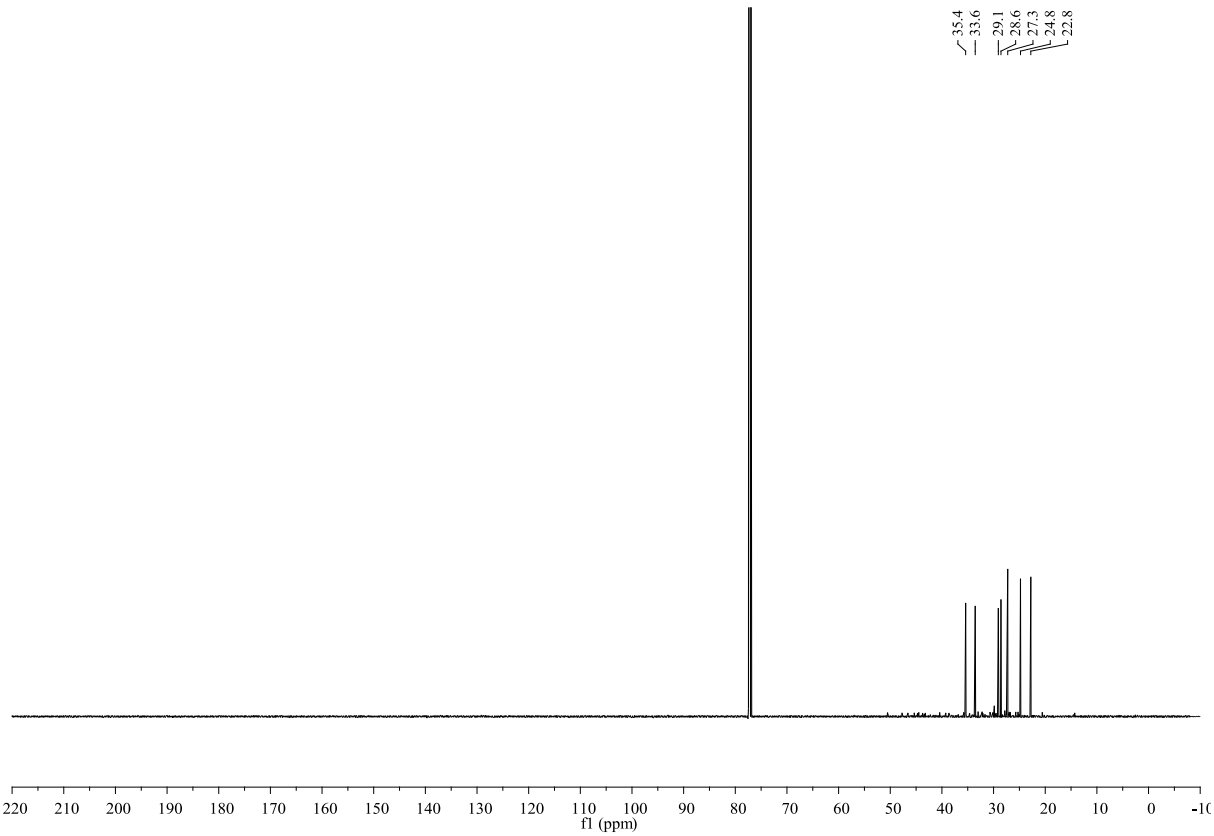


288 (^{1}H NMR, 600 MHz, $CDCl_3$)

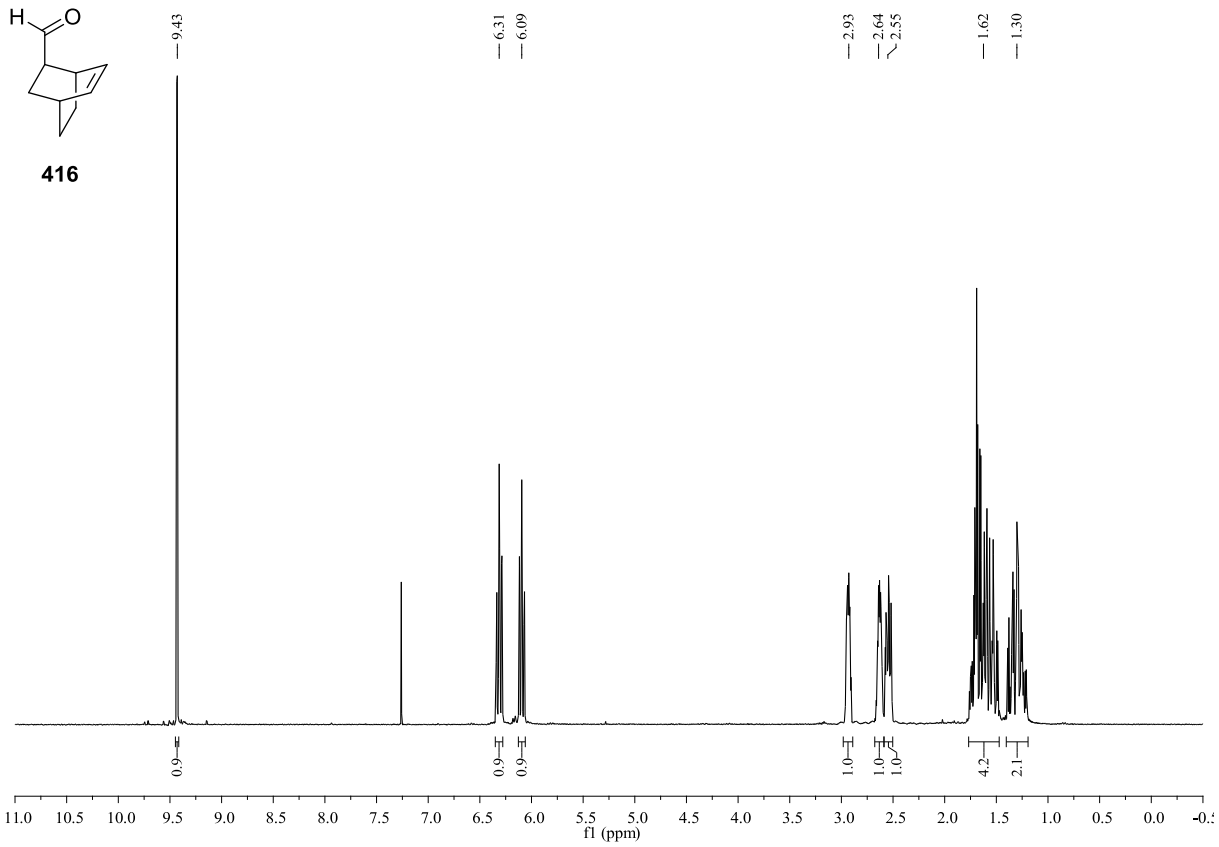


288

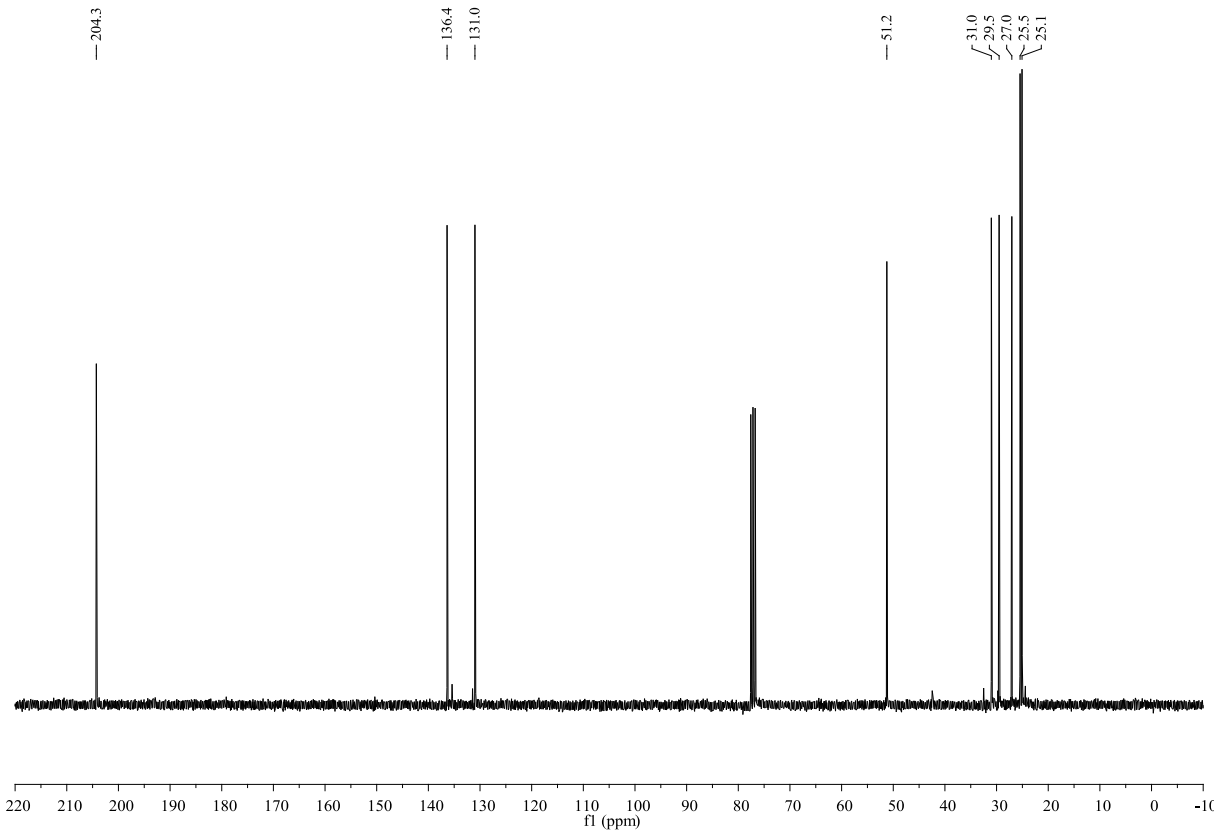
288 (^{13}C NMR, 150 MHz, $CDCl_3$)



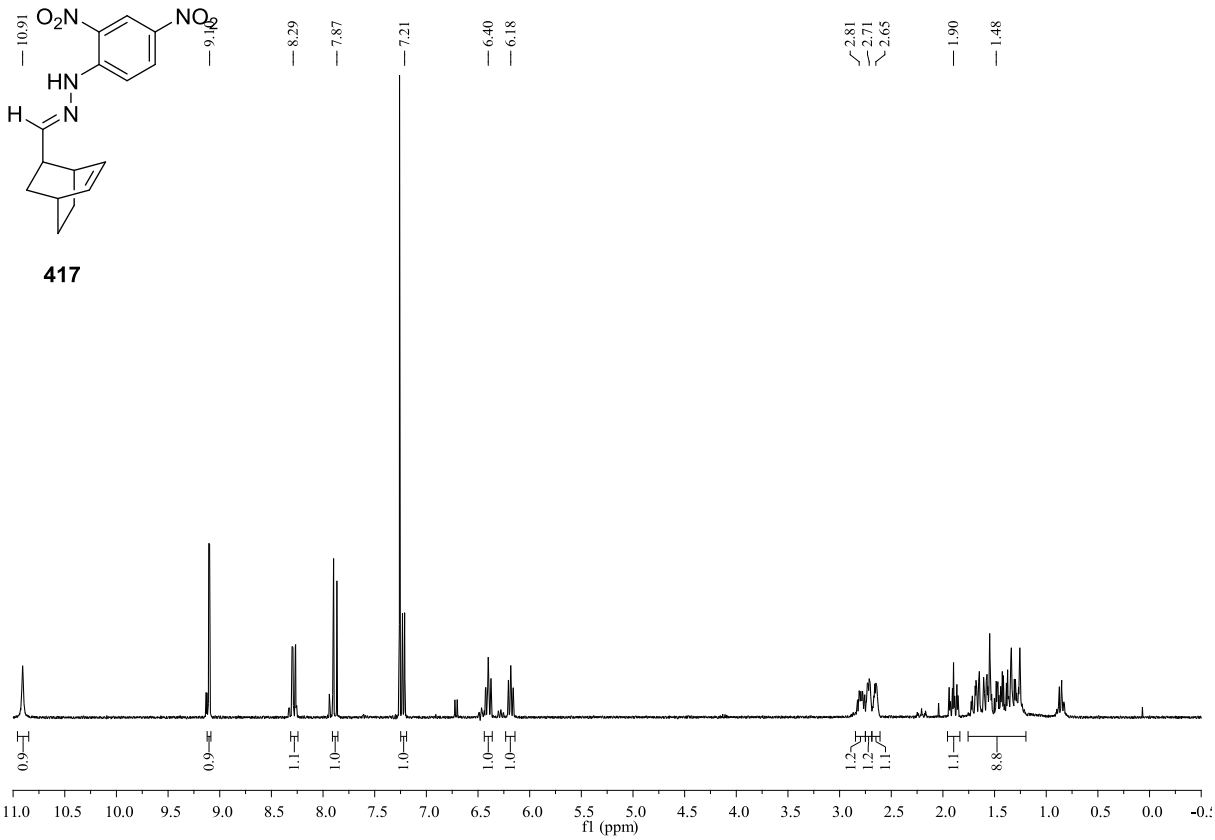
416 (^{1}H NMR, 300 MHz, $CDCl_3$)



416 (^{13}C NMR, 75 MHz, $CDCl_3$)

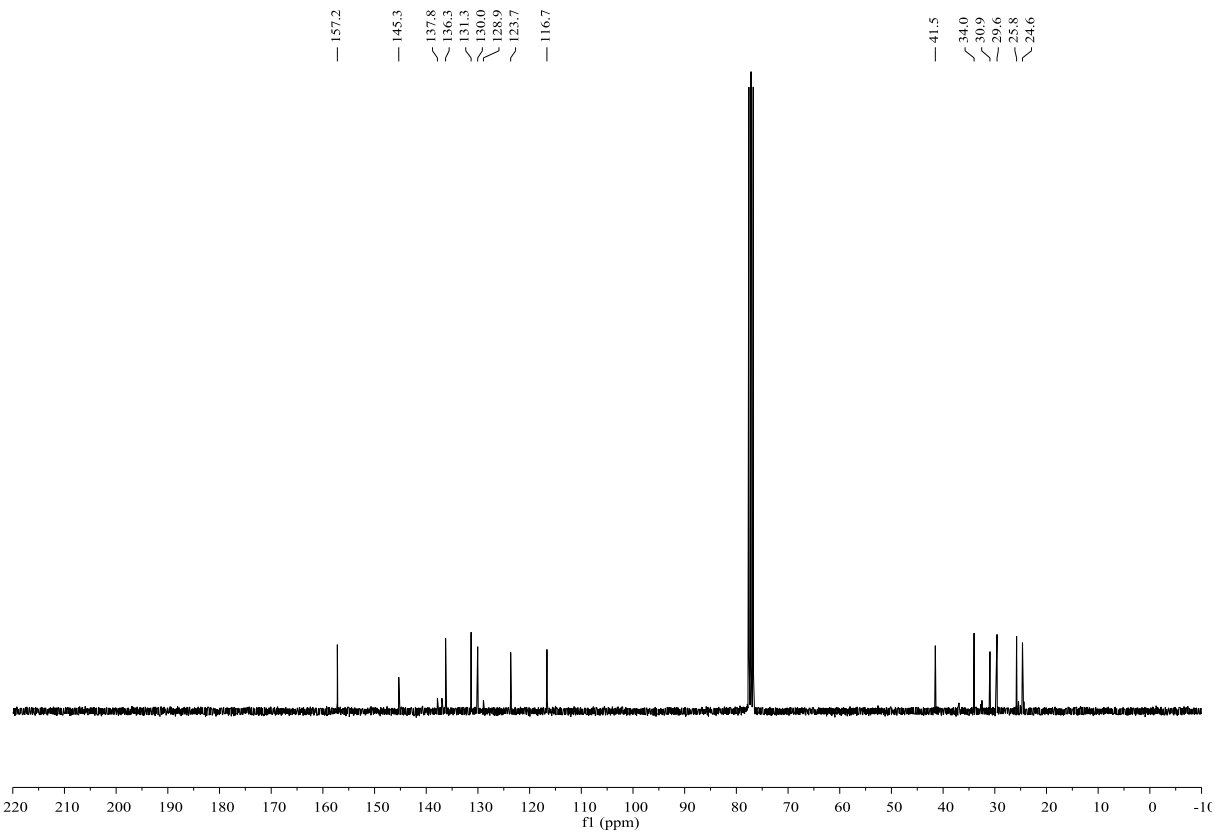


417 (^{1}H NMR, 300 MHz, $CDCl_3$)

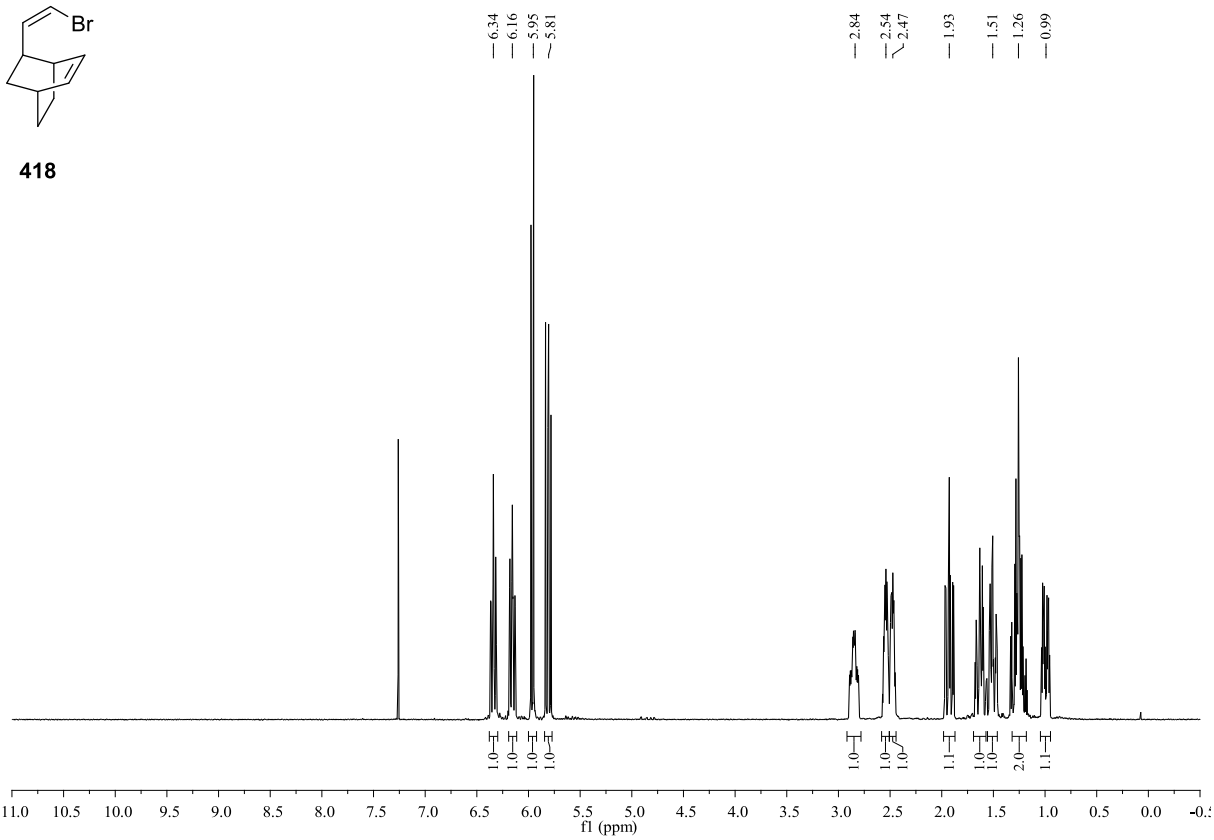


417

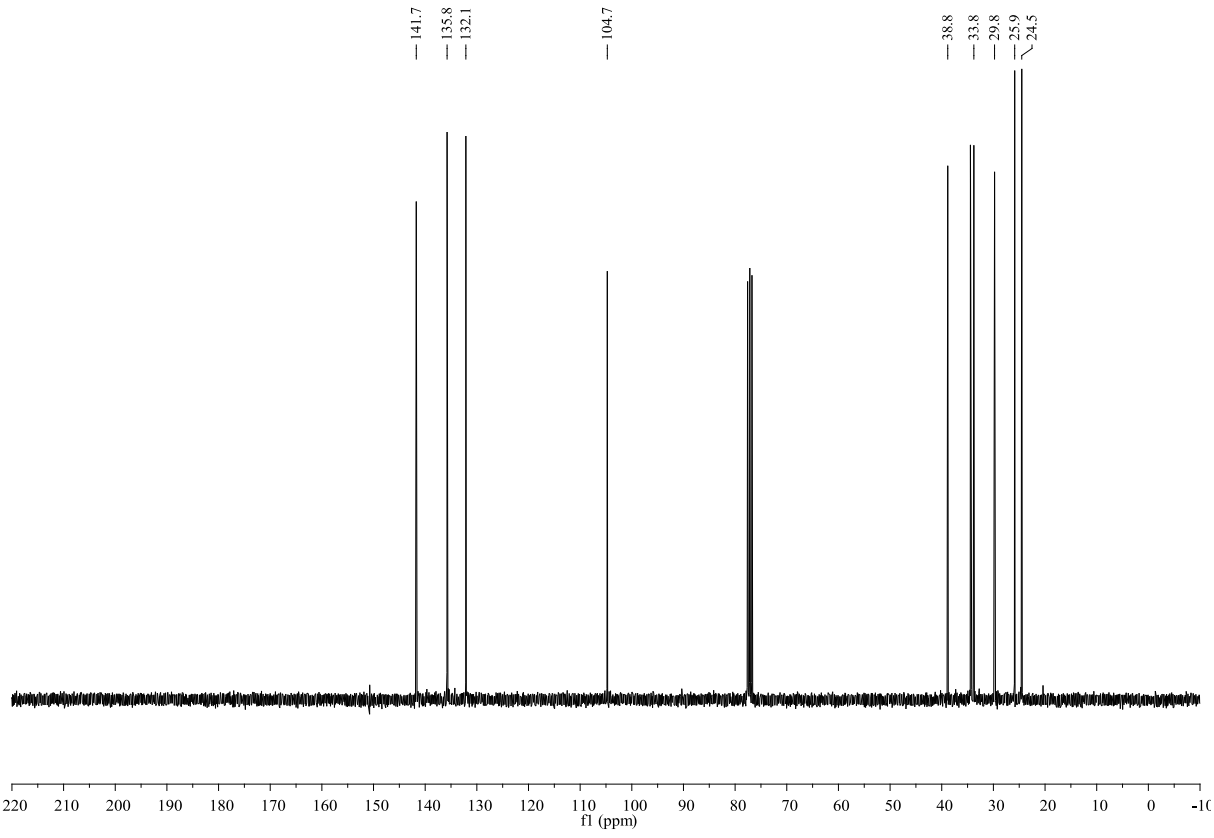
417 (^{13}C NMR, 75 MHz, $CDCl_3$)



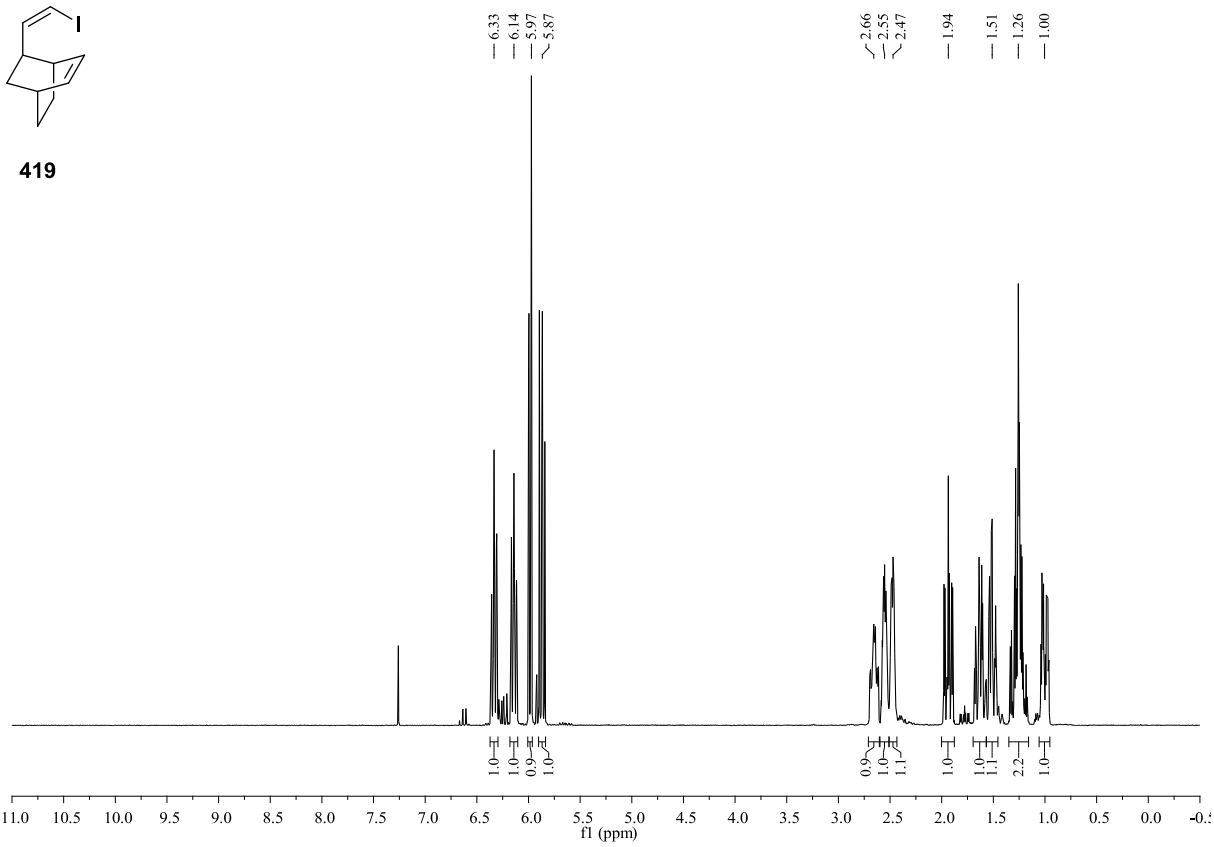
418 (^{1}H NMR, 300 MHz, $CDCl_3$)



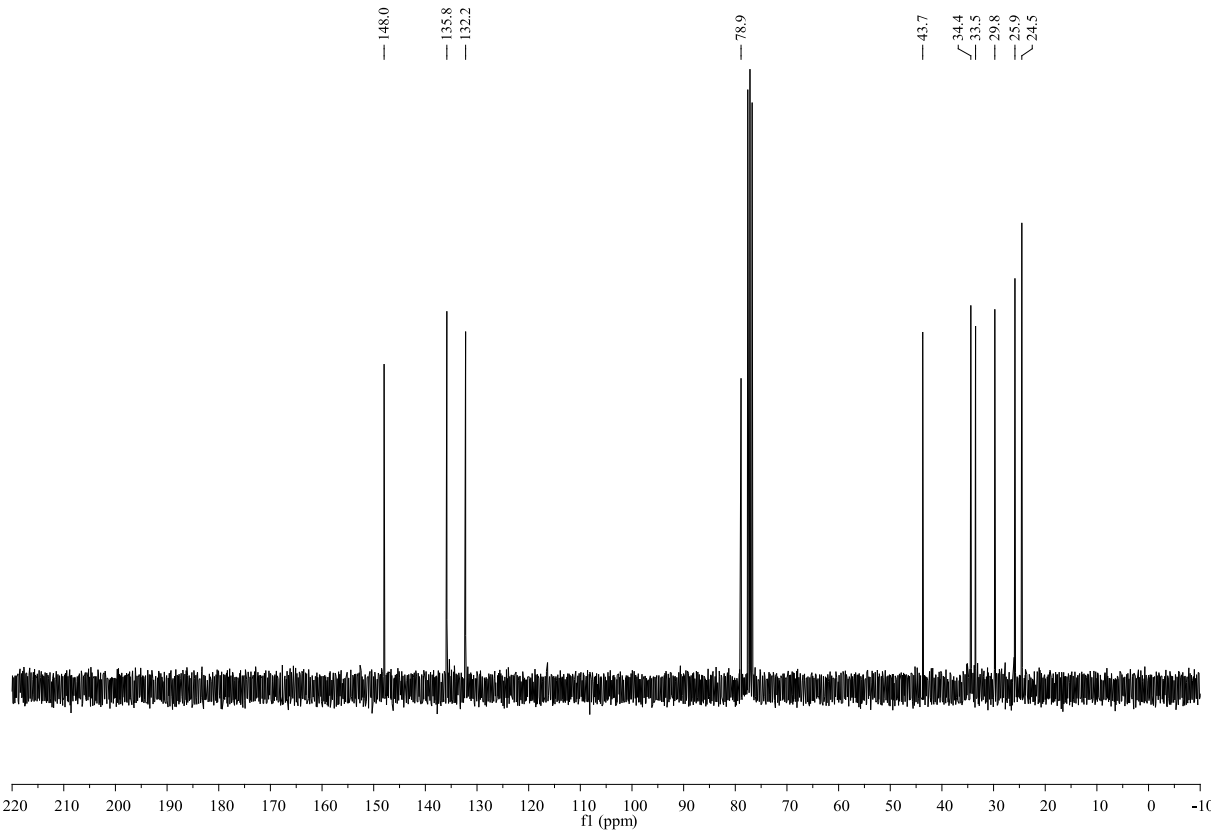
418 (^{13}C NMR, 75 MHz, $CDCl_3$)



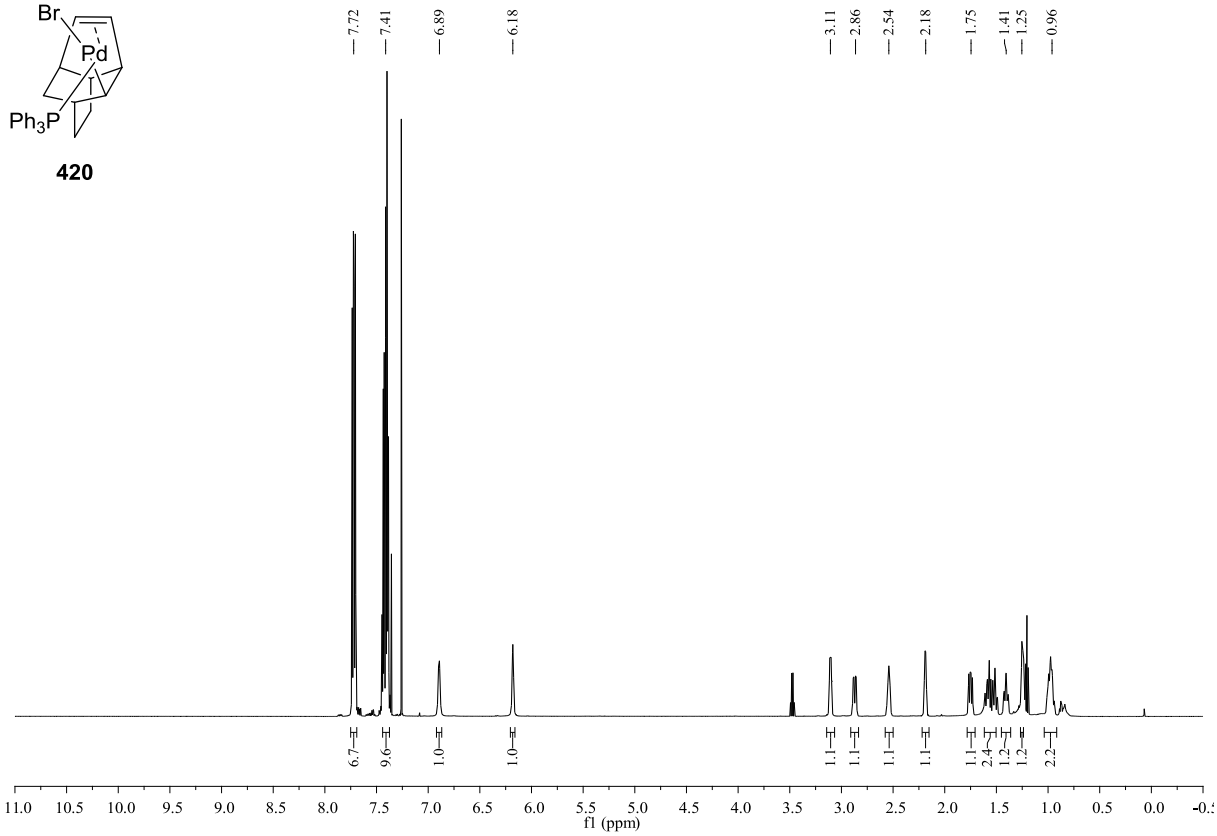
419 (^{1}H NMR, 300 MHz, $CDCl_3$)



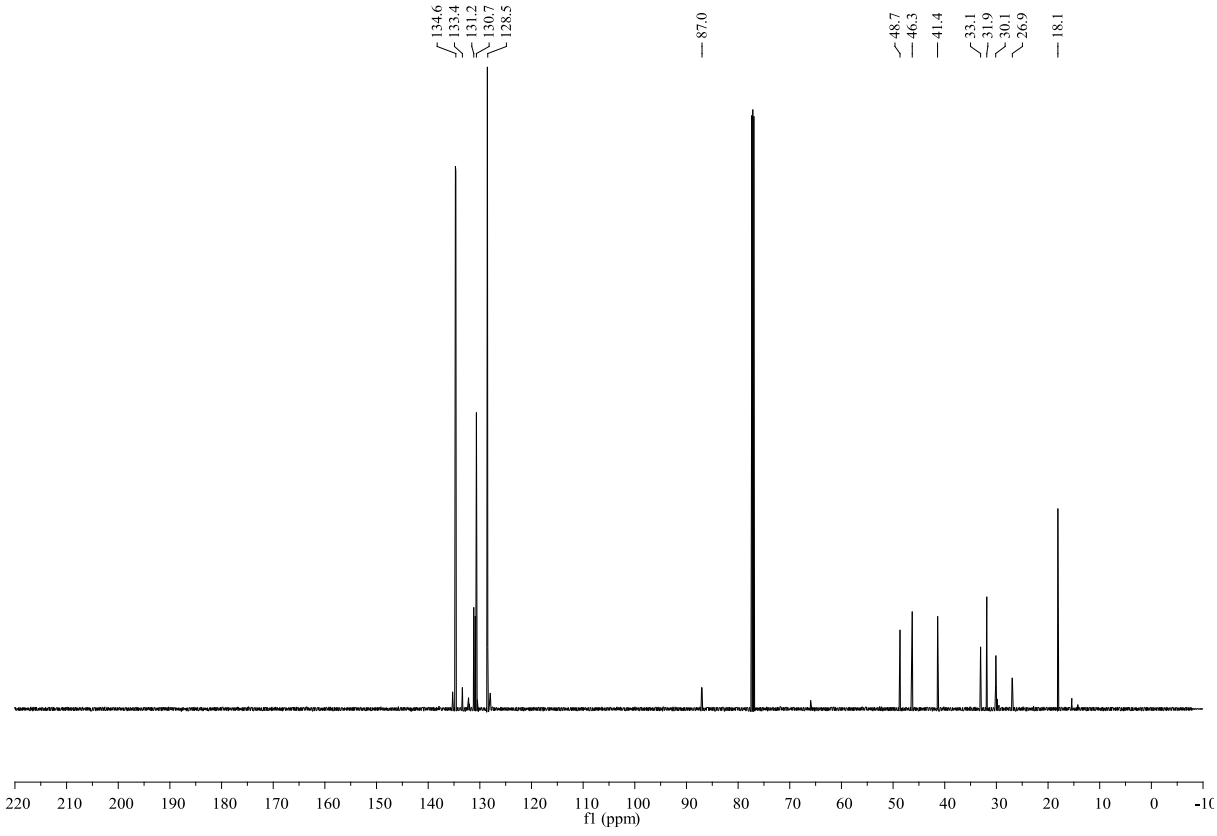
419 (^{13}C NMR, 75 MHz, $CDCl_3$)



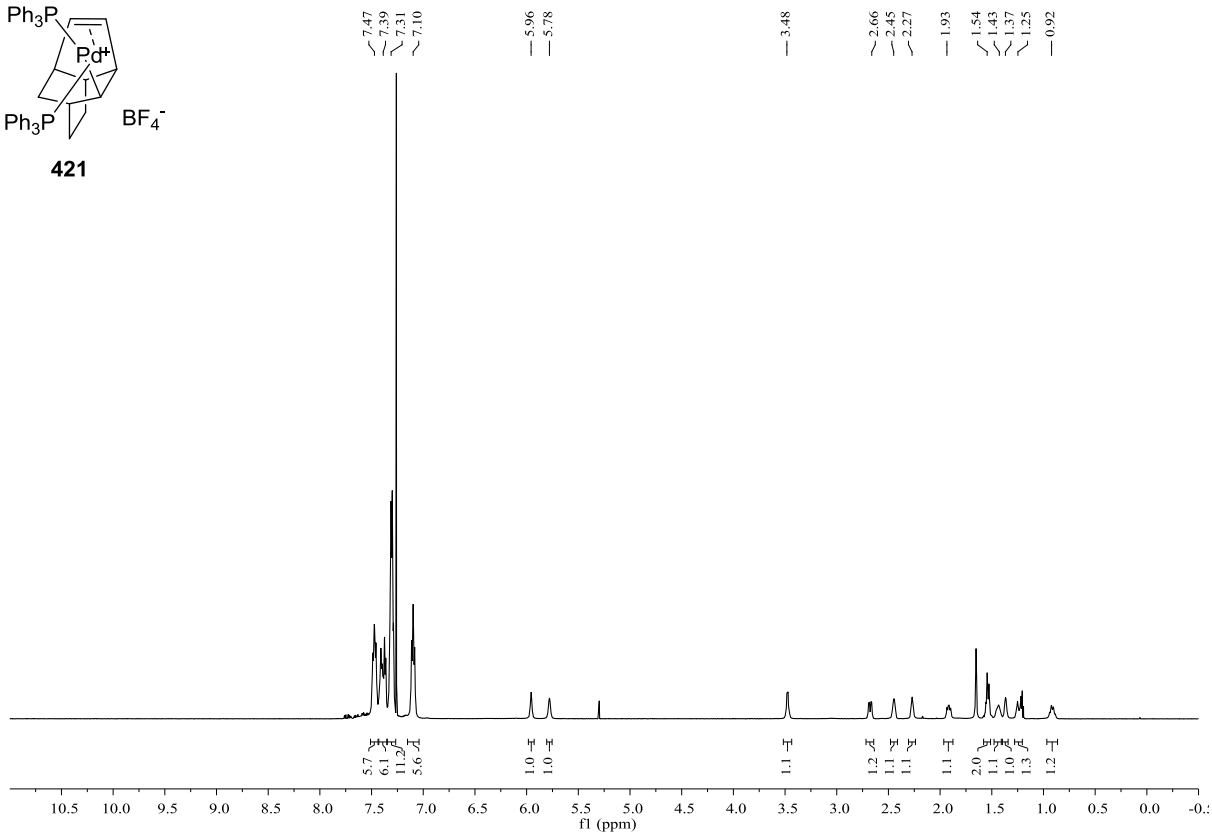
420 (^{1}H NMR, 600 MHz, $CDCl_3$)



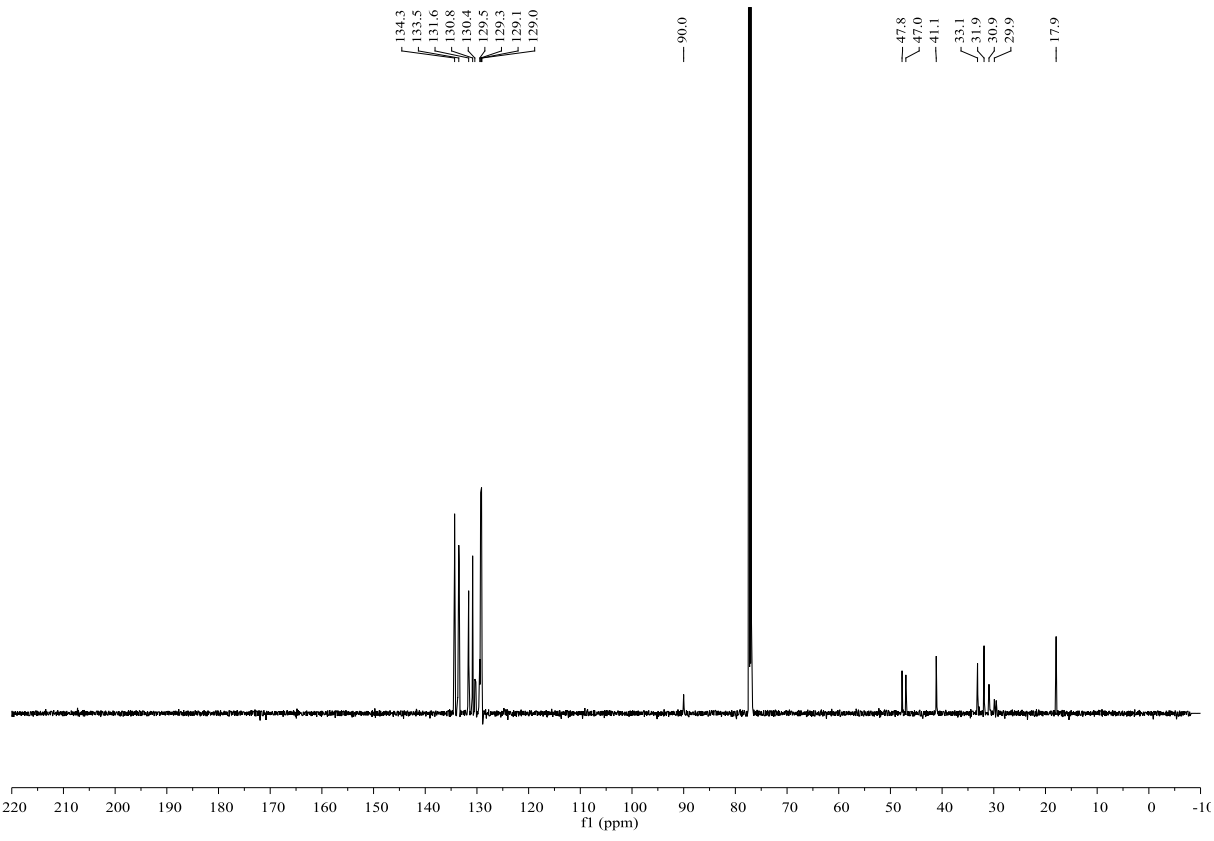
420 (^{13}C NMR, 150 MHz, $CDCl_3$)



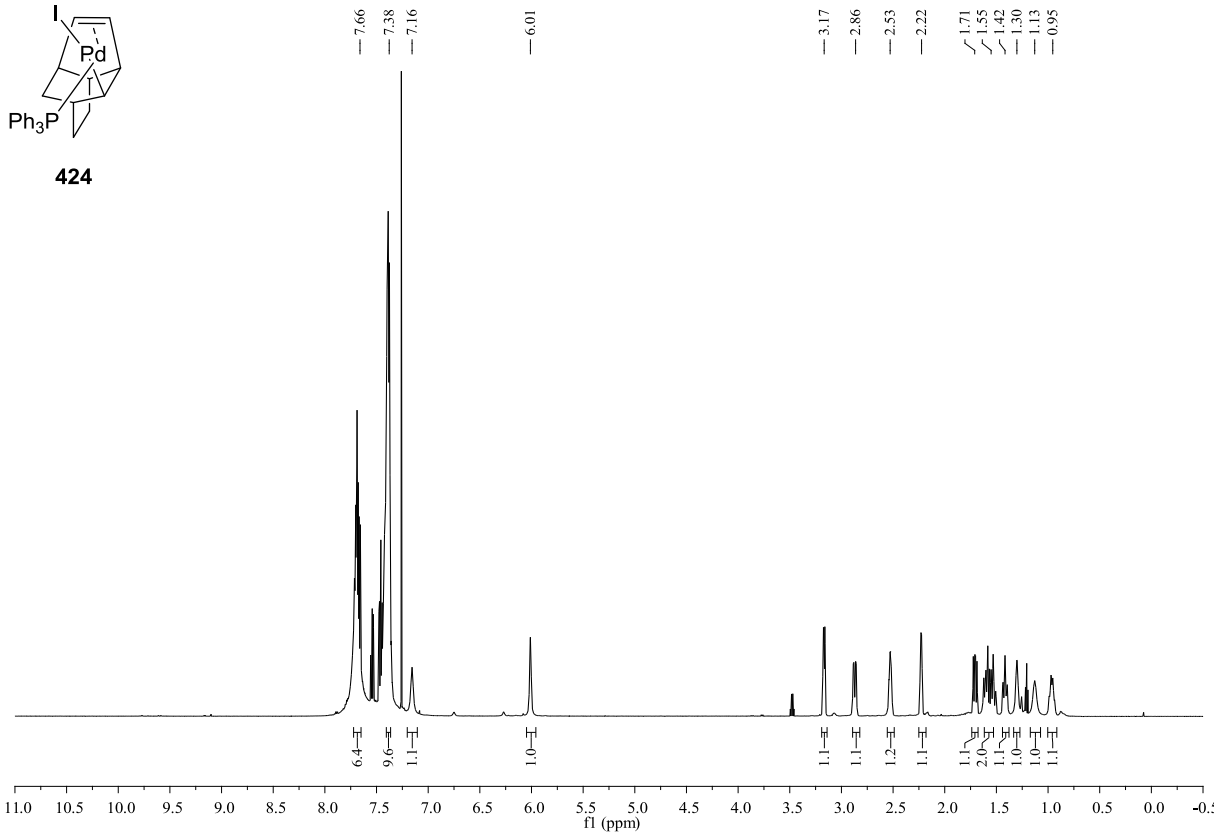
421 (^{1}H NMR, 600 MHz, $CDCl_3$)



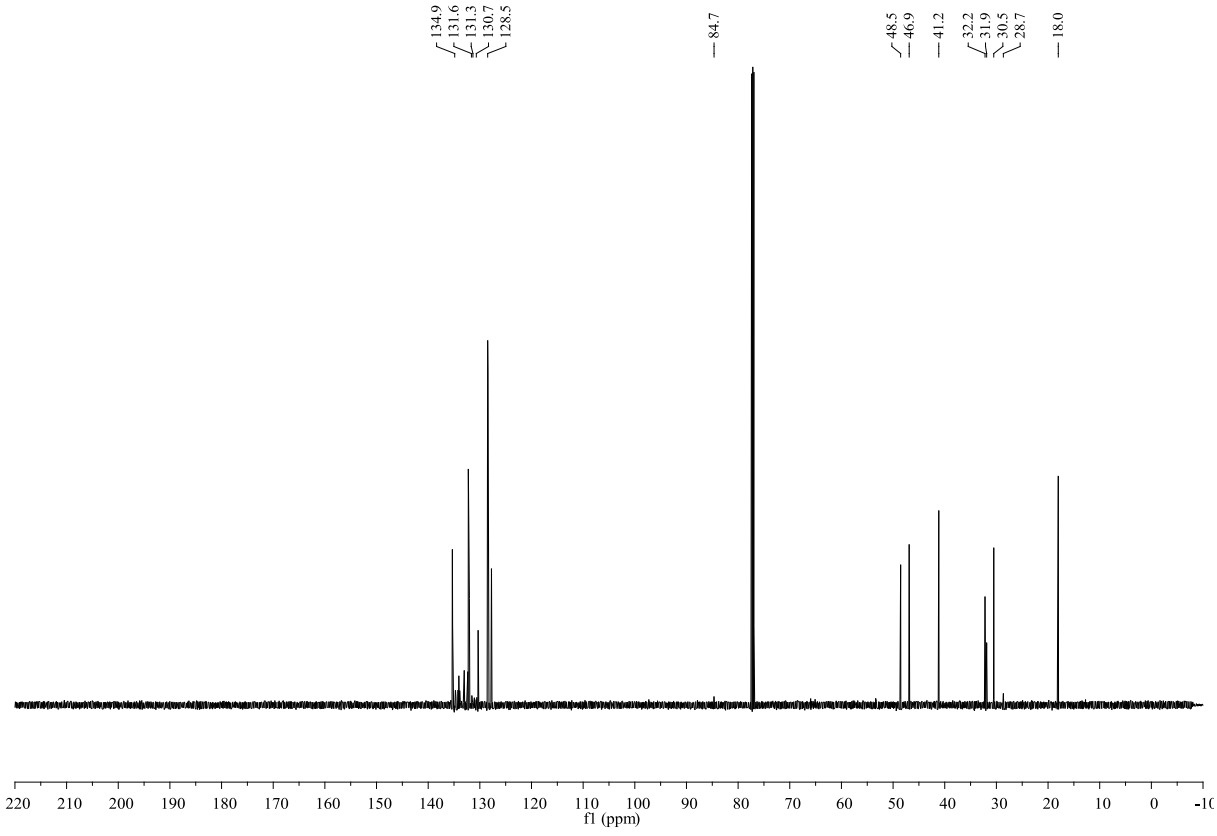
421 (^{13}C NMR, 150 MHz, $CDCl_3$)



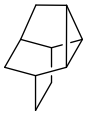
424 (^{1}H NMR, 600 MHz, $CDCl_3$)



424 (^{13}C NMR, 150 MHz, $CDCl_3$)

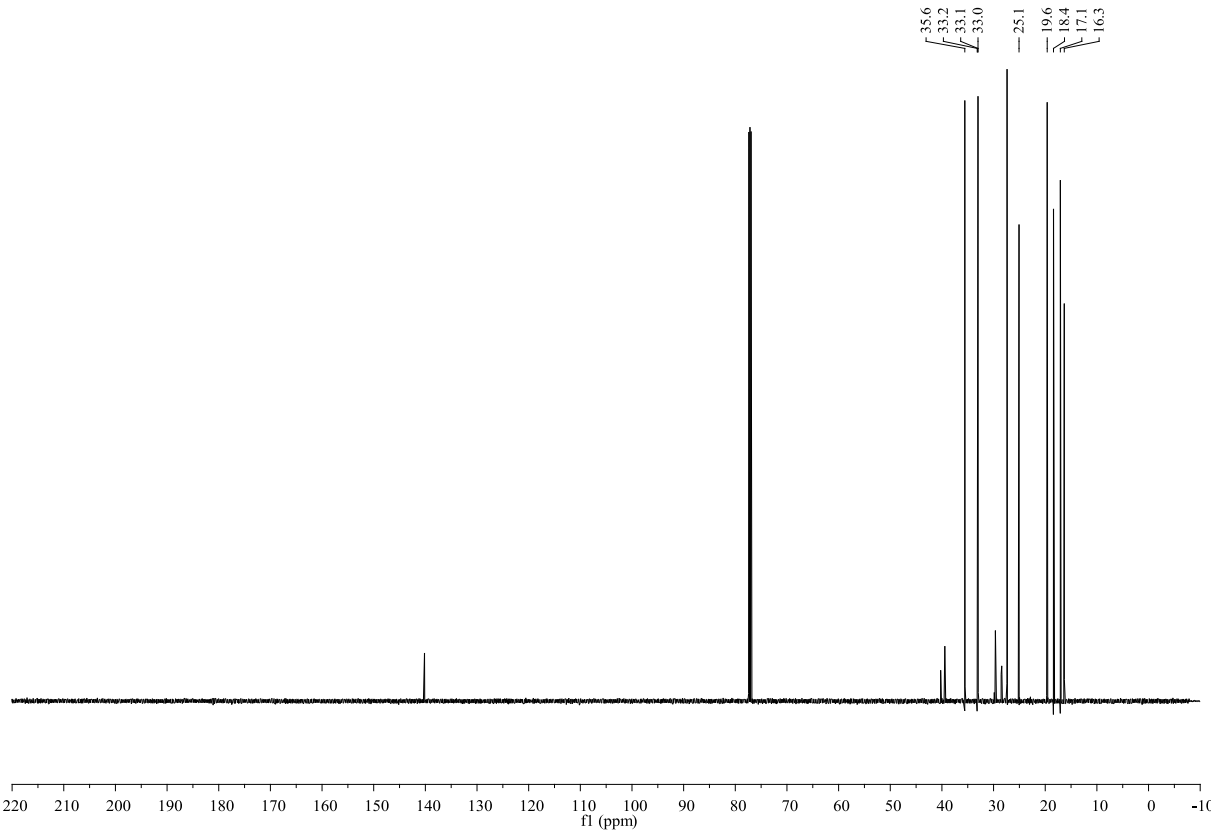


425 (^{1}H NMR, 600 MHz, $CDCl_3$)

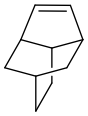


425

425 (^{13}C NMR, 150 MHz, $CDCl_3$)

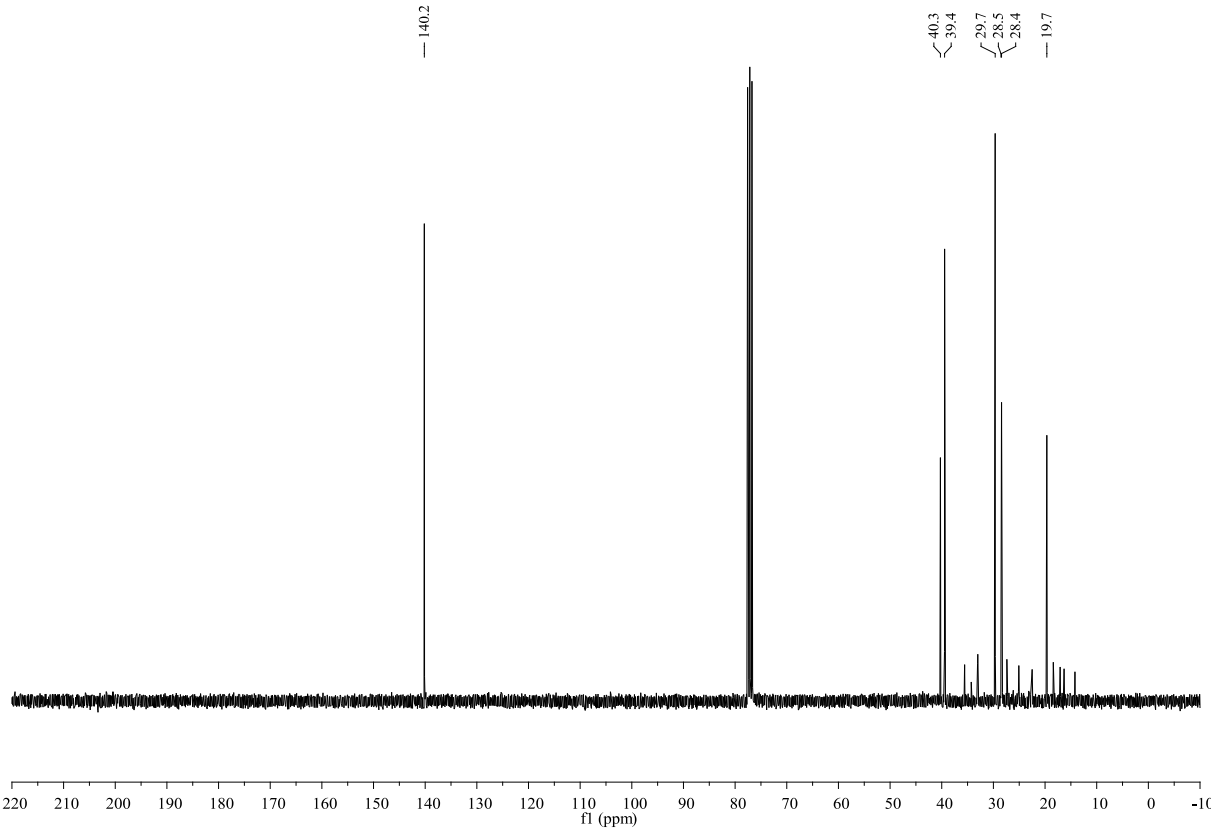


426 (^{1}H NMR, 600 MHz, $CDCl_3$)

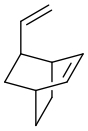


426

426 (^{13}C NMR, 75 MHz, $CDCl_3$)

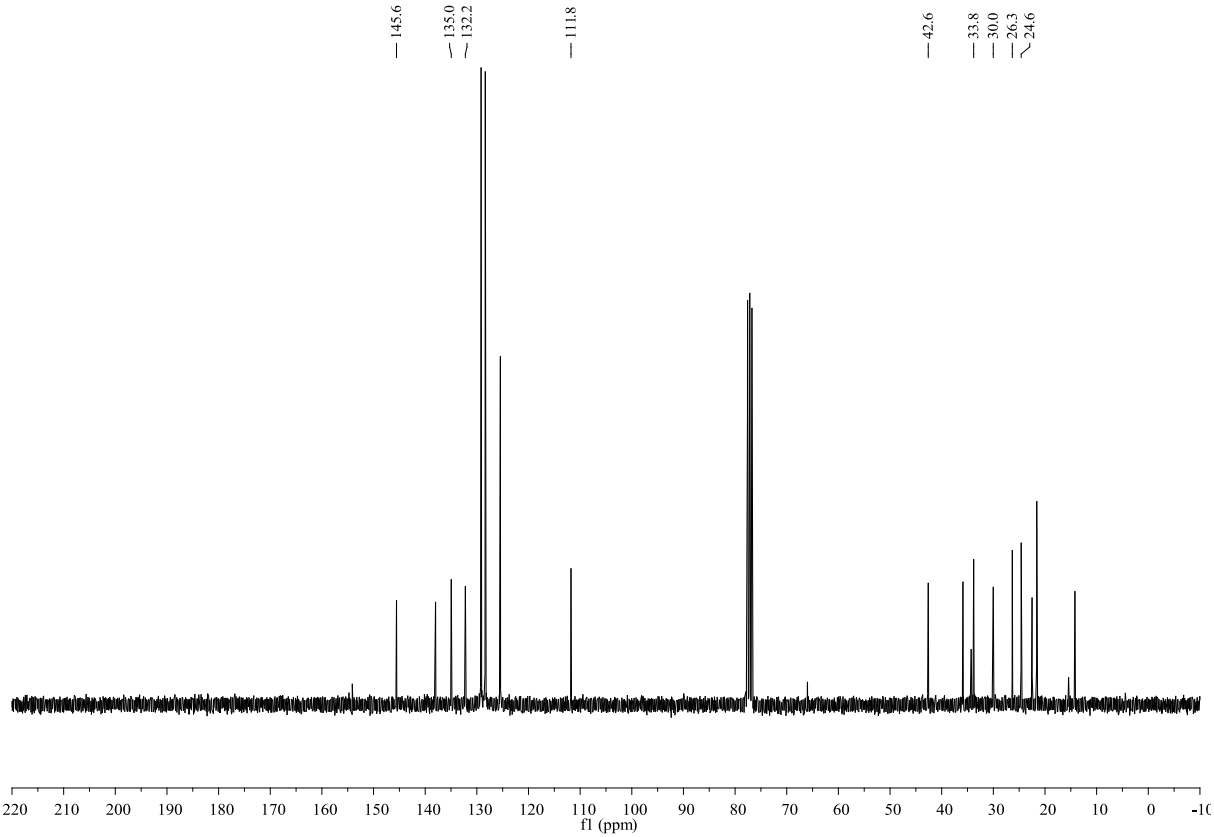


427 (^{1}H NMR, 300 MHz, $CDCl_3$)

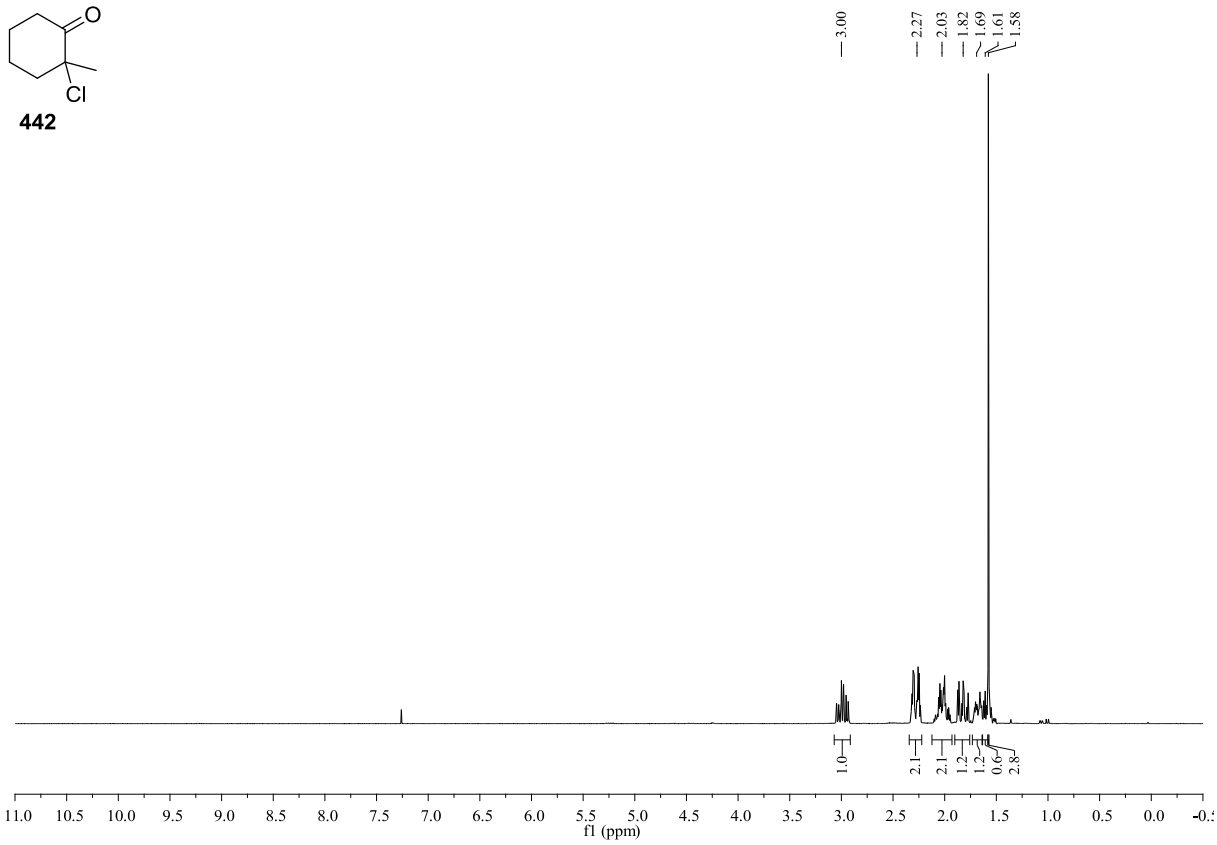


427

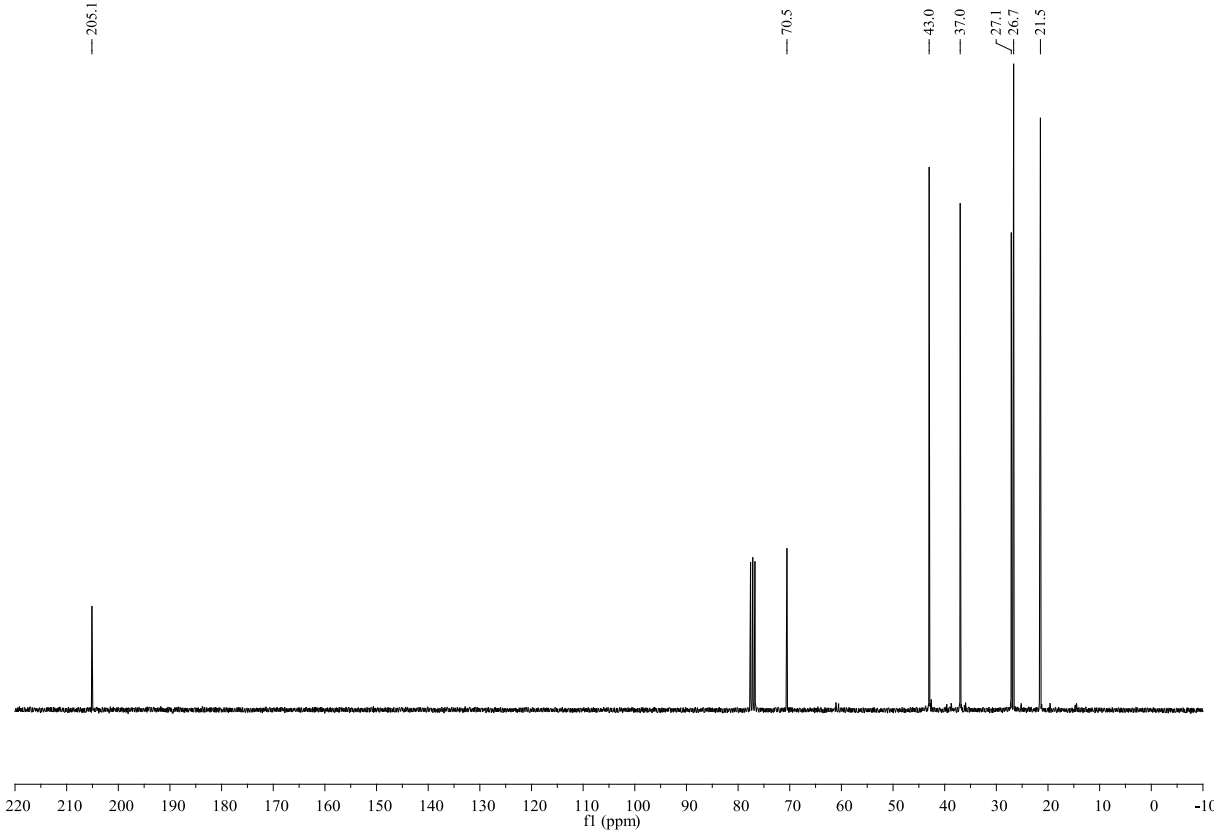
427 (^{13}C NMR, 75 MHz, $CDCl_3$)



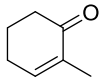
442 (^{1}H NMR, 300 MHz, $CDCl_3$)



442 (^{13}C NMR, 75 MHz, $CDCl_3$)

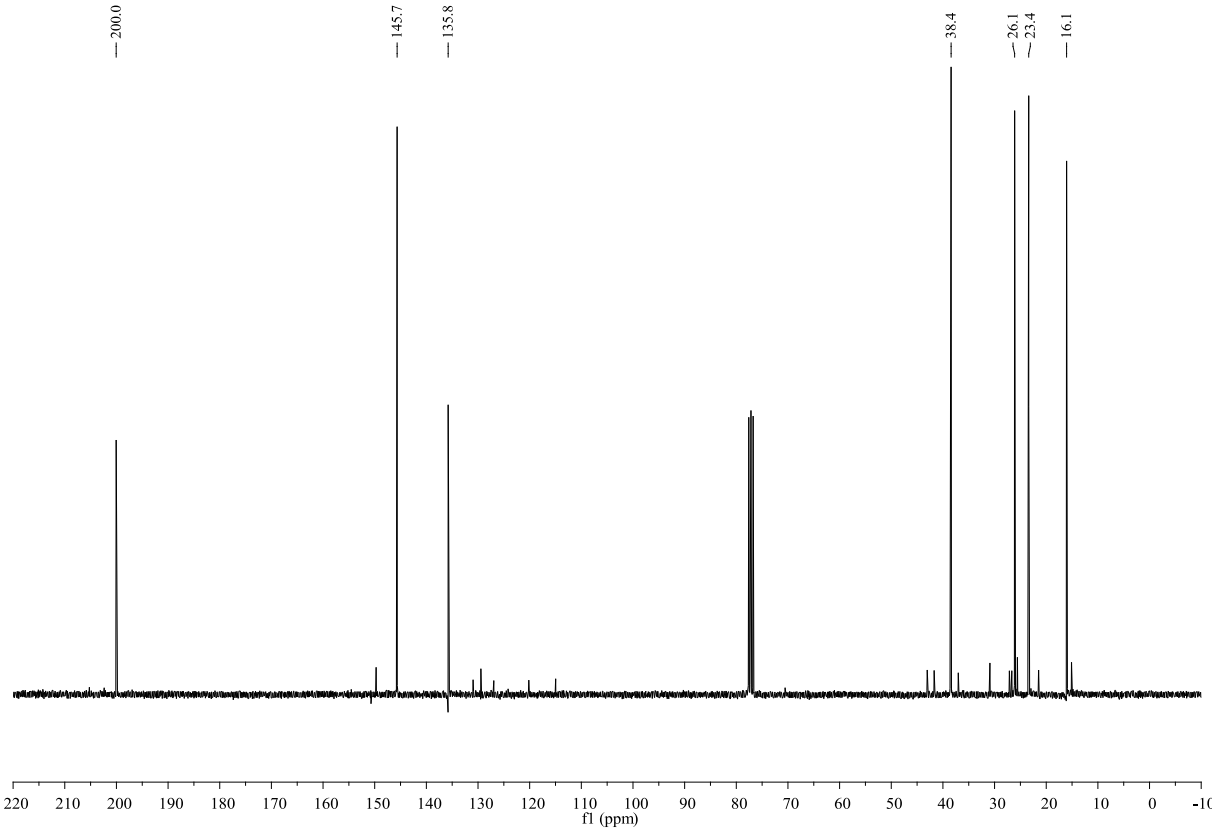


303 (^{1}H NMR, 300 MHz, $CDCl_3$)

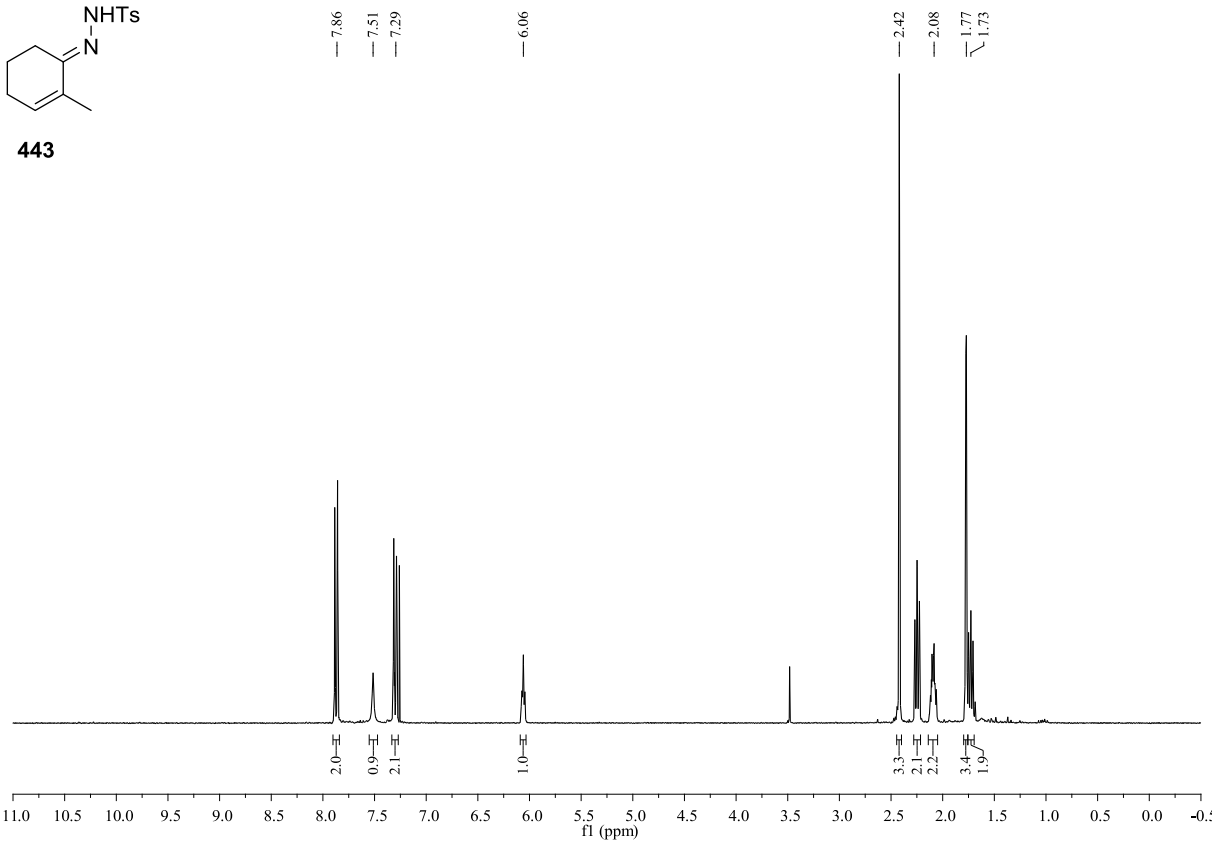


303

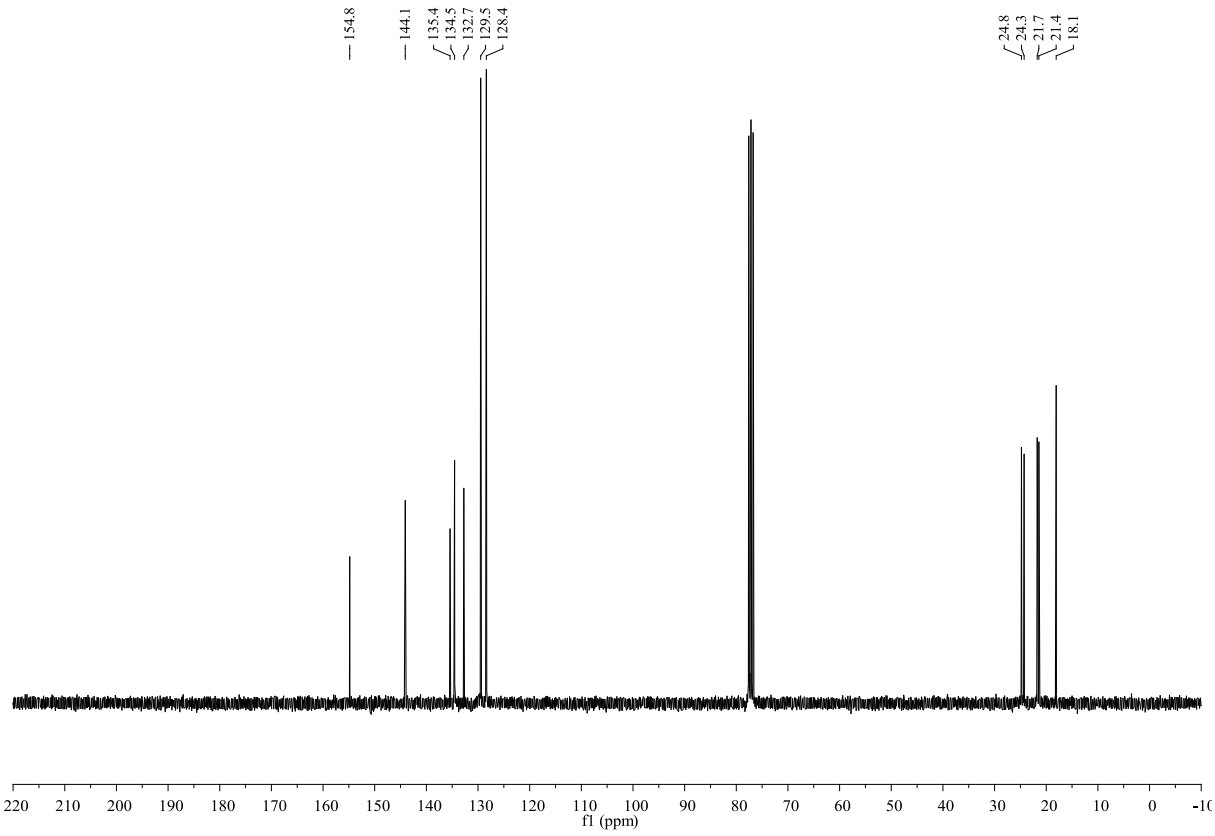
303 (^{13}C NMR, 75 MHz, $CDCl_3$)



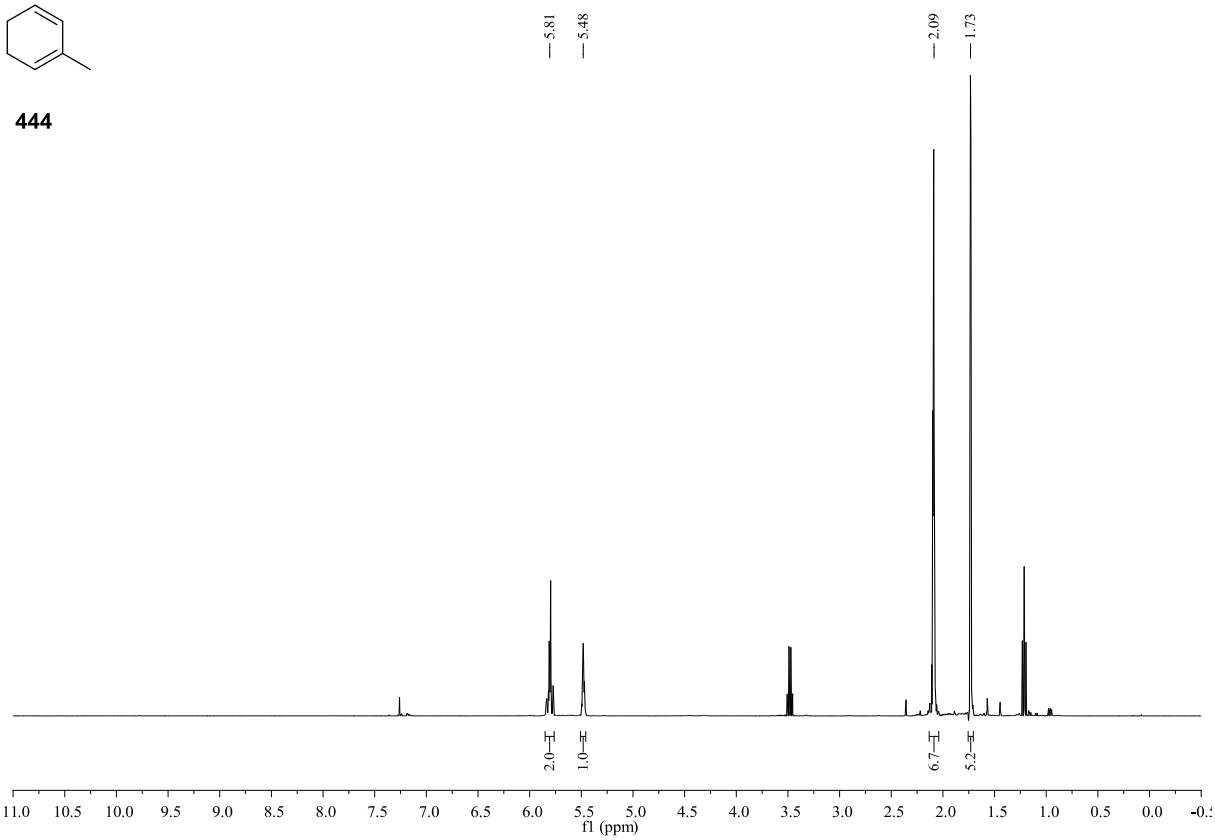
443 (^{1}H NMR, 300 MHz, $CDCl_3$)



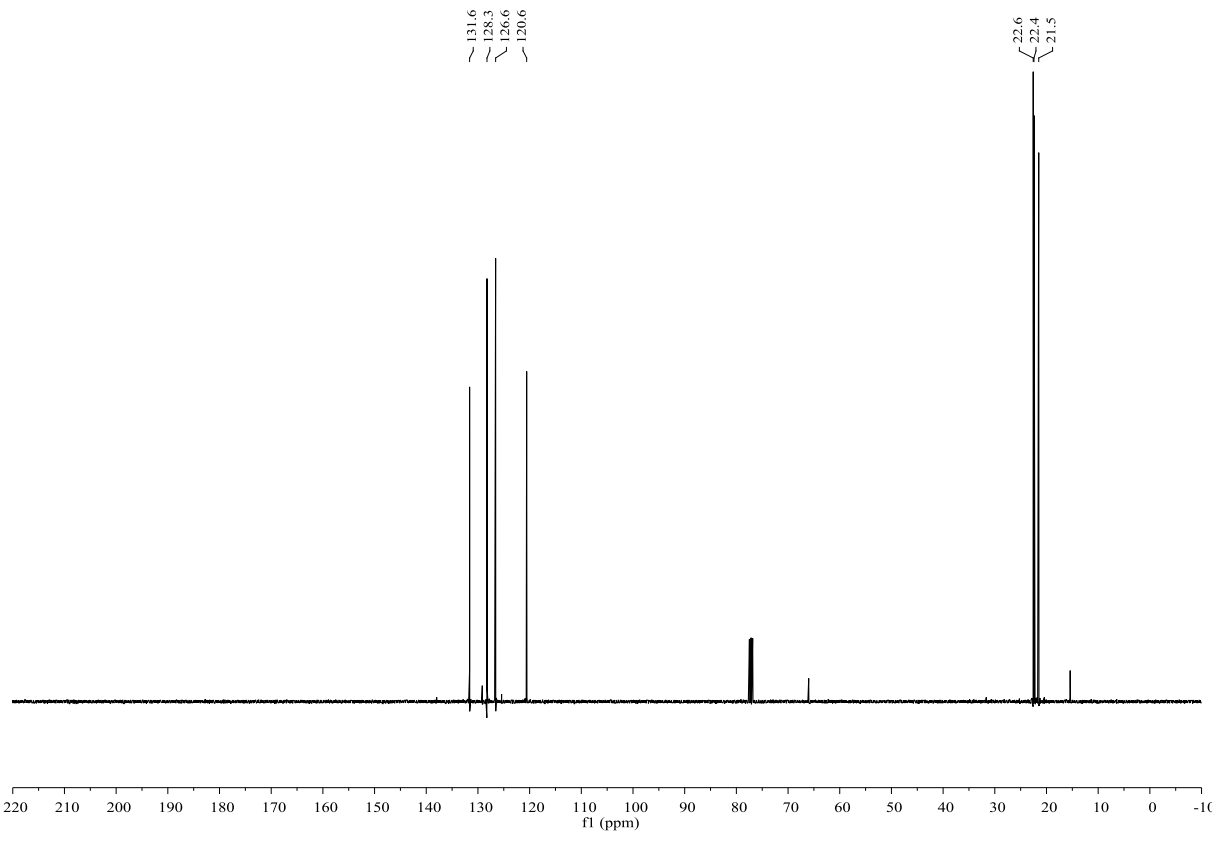
443 (^{13}C NMR, 75 MHz, $CDCl_3$)



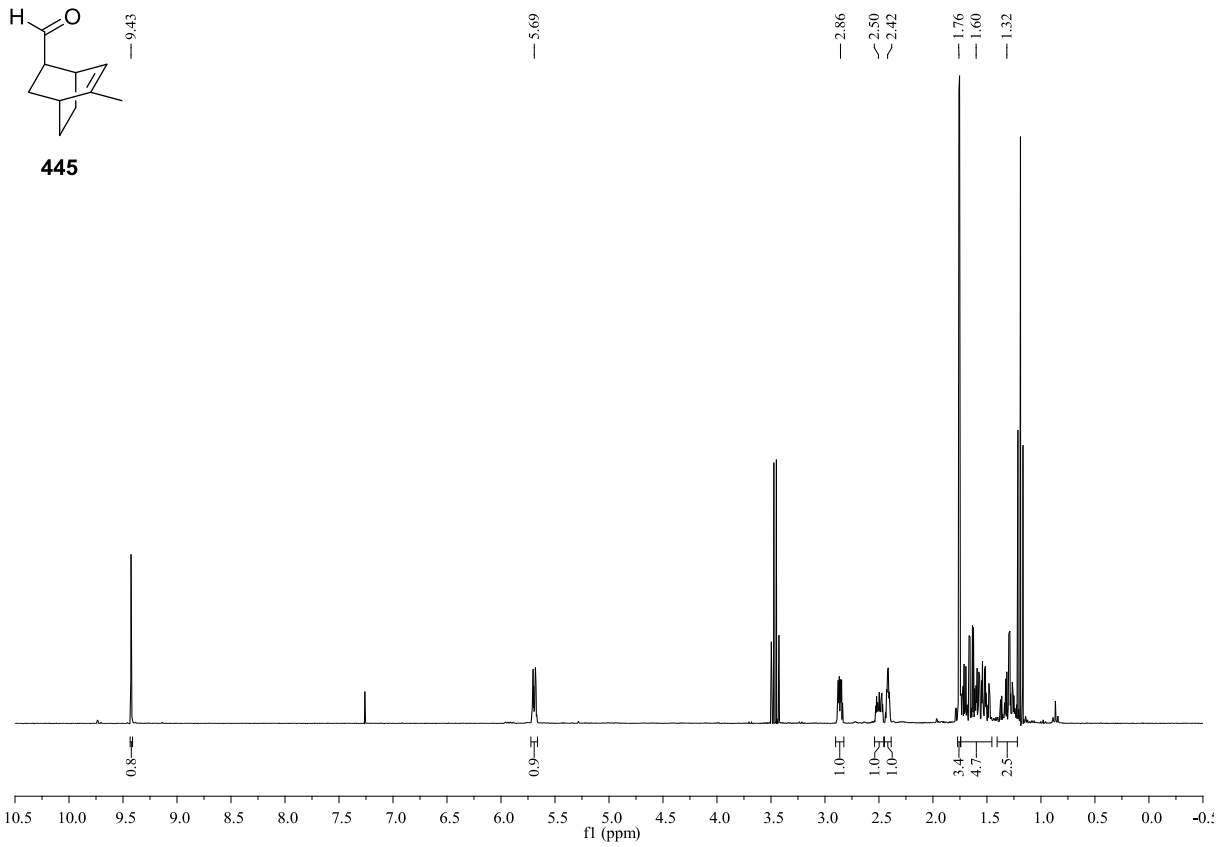
444 (^{1}H NMR, 400 MHz, $CDCl_3$)



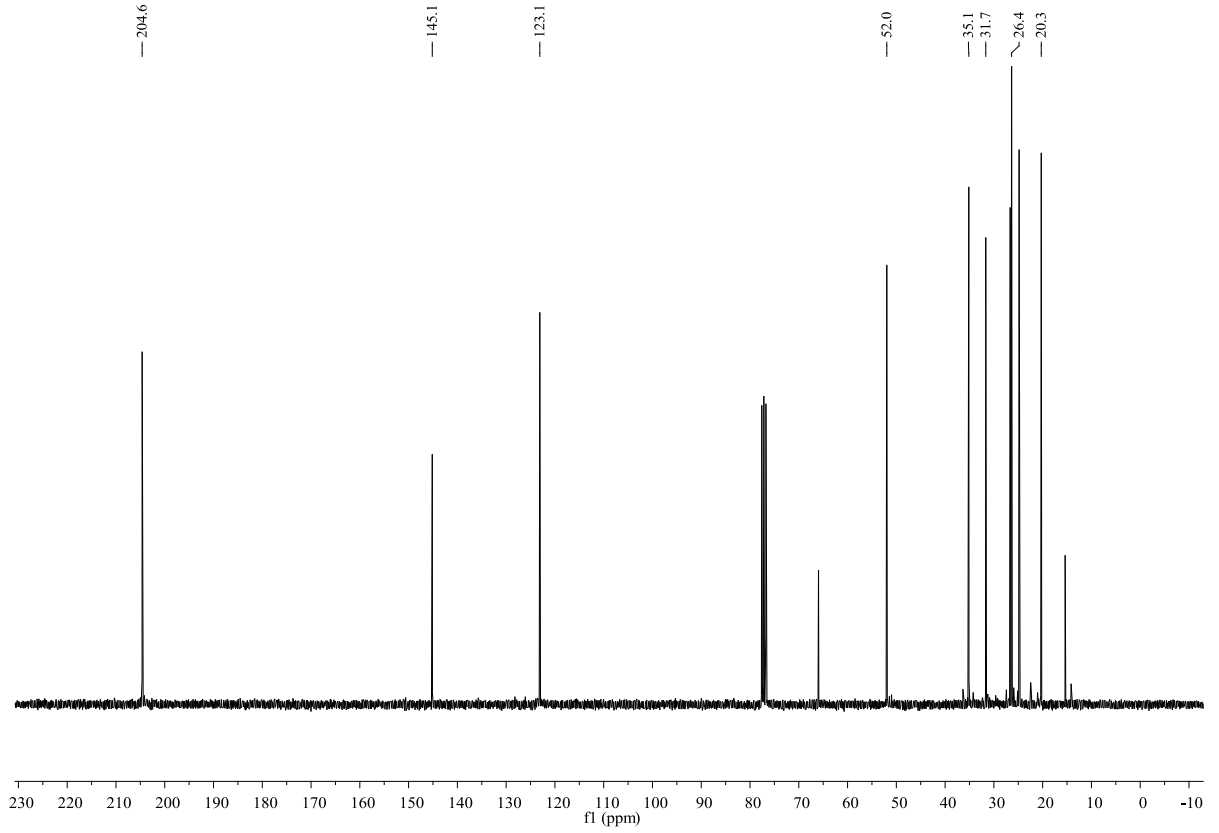
444 (^{13}C NMR, 100 MHz, $CDCl_3$)



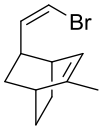
445 (^{1}H NMR, 300 MHz, $CDCl_3$)



445 (^{13}C NMR, 75 MHz, $CDCl_3$)

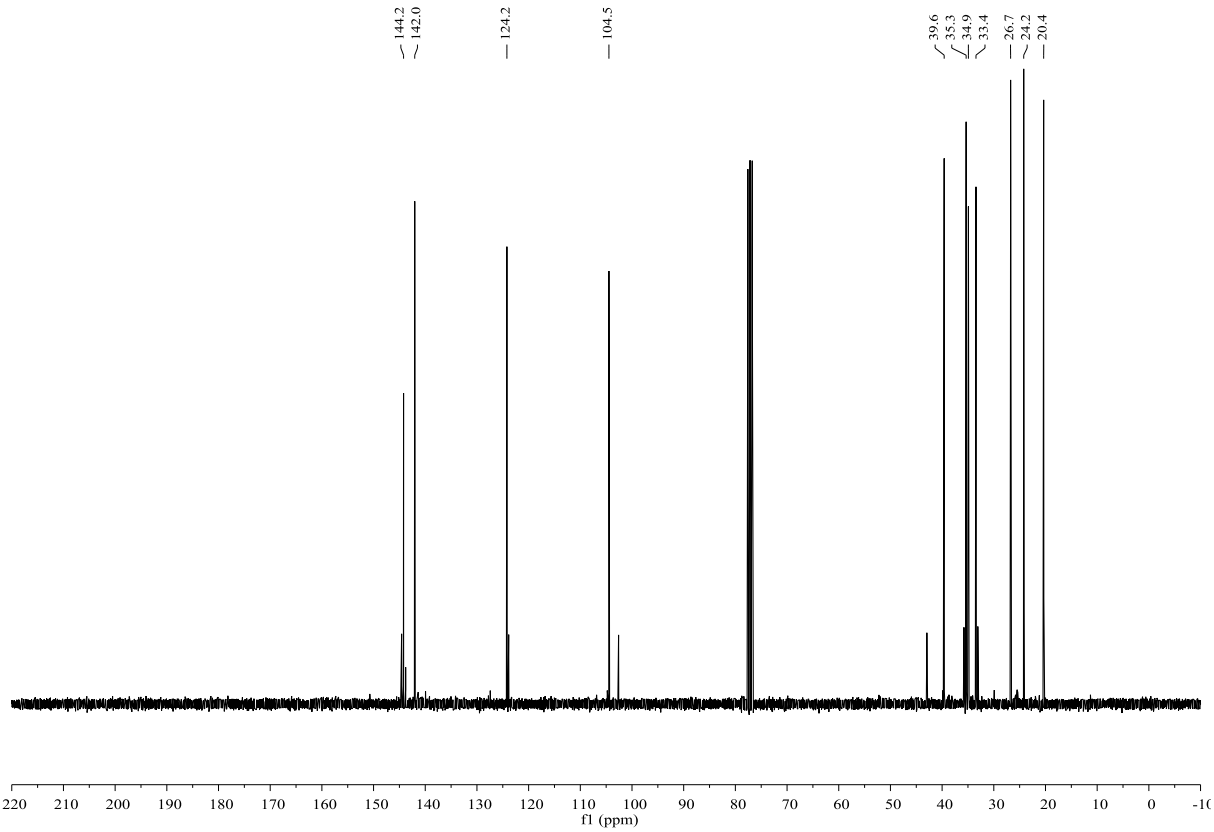


438 (^{1}H NMR, 300 MHz, $CDCl_3$)

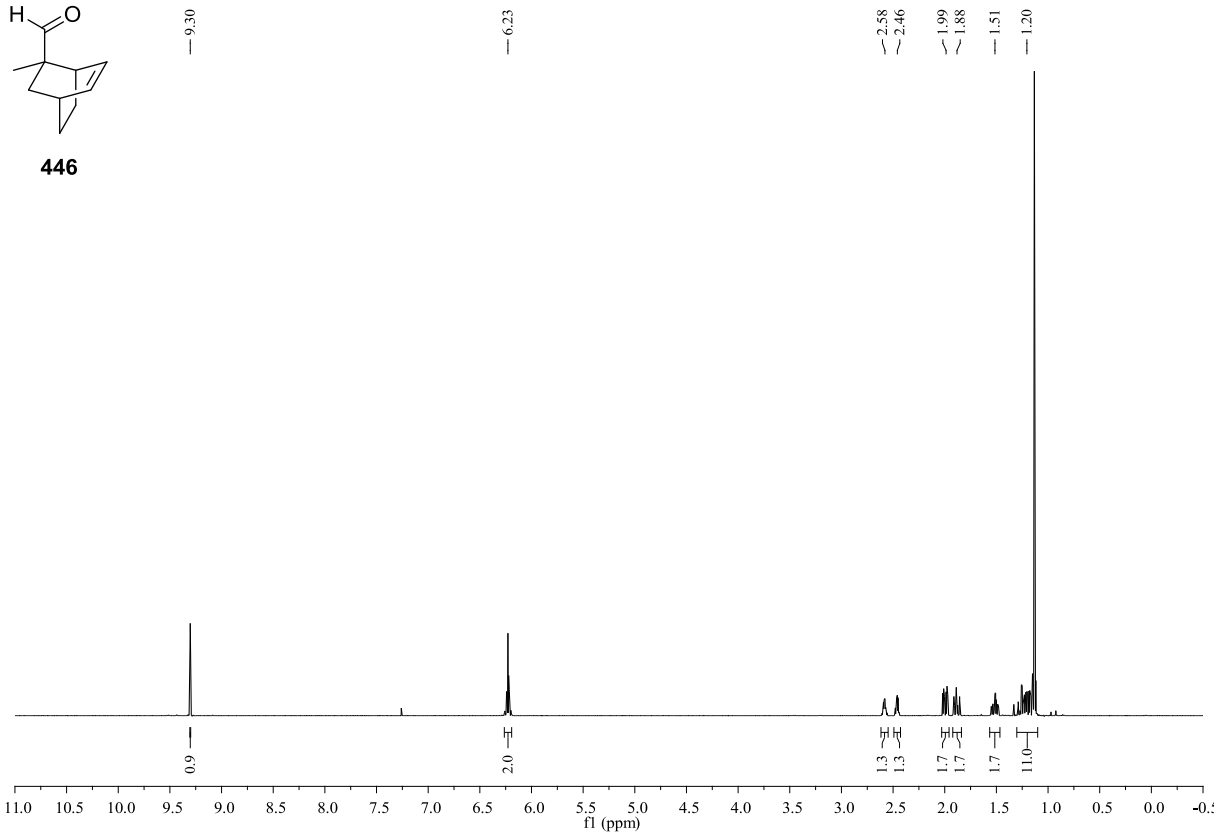


438

438 (^{13}C NMR, 75 MHz, $CDCl_3$)

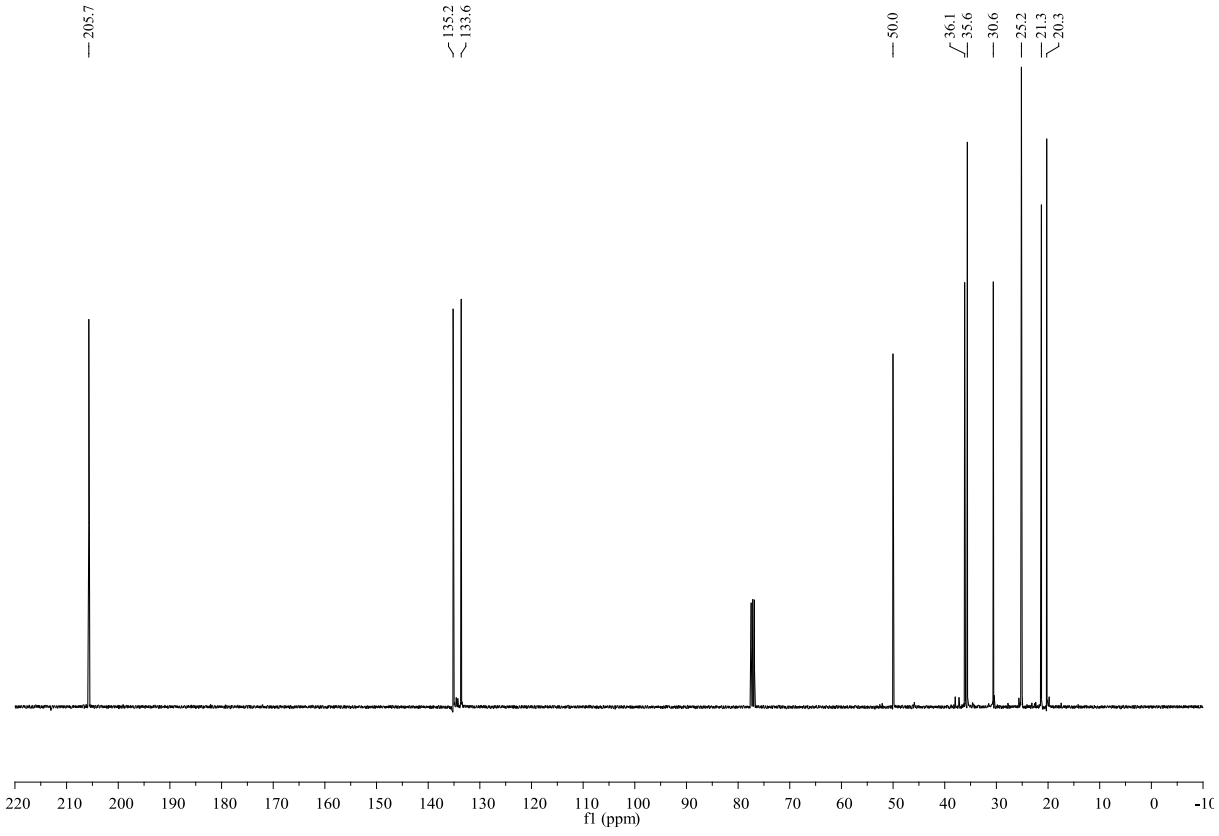


446 (^{1}H NMR, 400 MHz, $CDCl_3$)

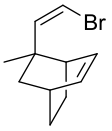


446

446 (^{13}C NMR, 100 MHz, $CDCl_3$)

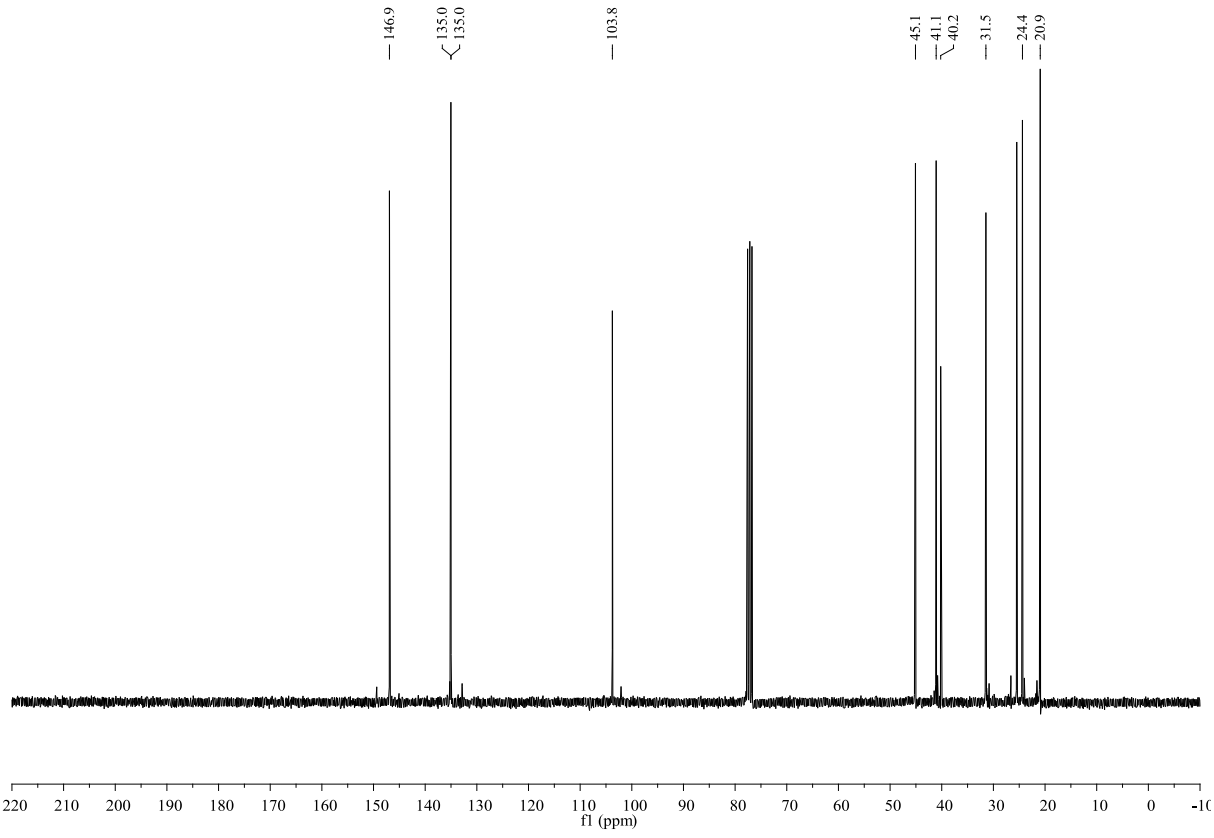


439 (^{1}H NMR, 300 MHz, $CDCl_3$)

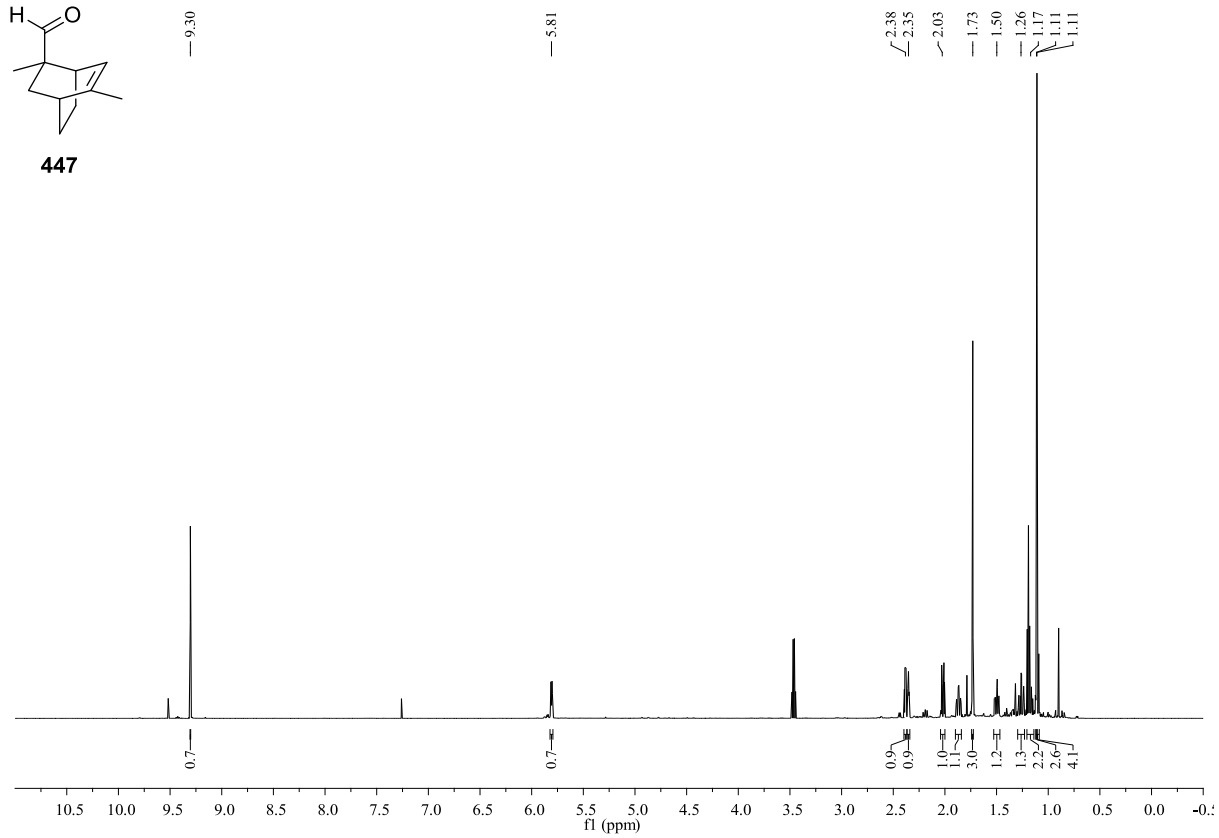


439

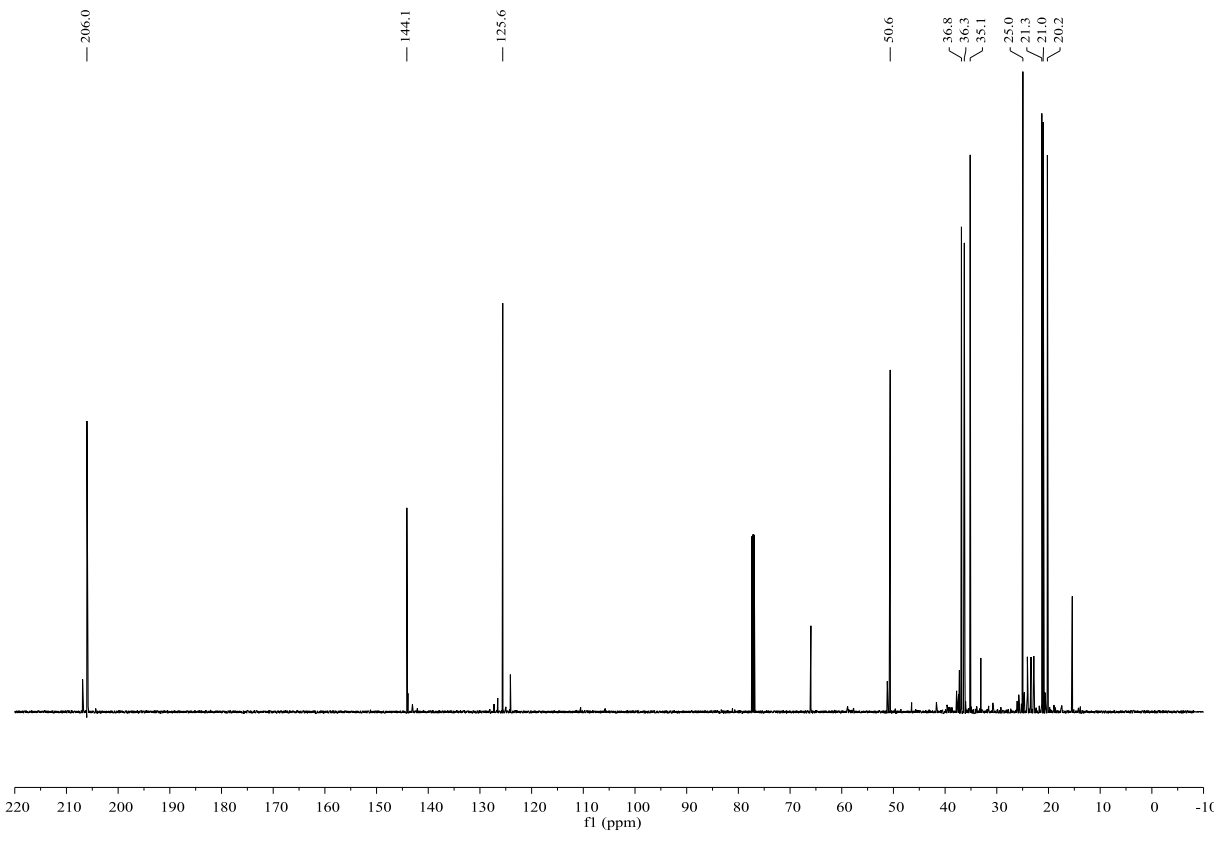
439 (^{13}C NMR, 75 MHz, $CDCl_3$)



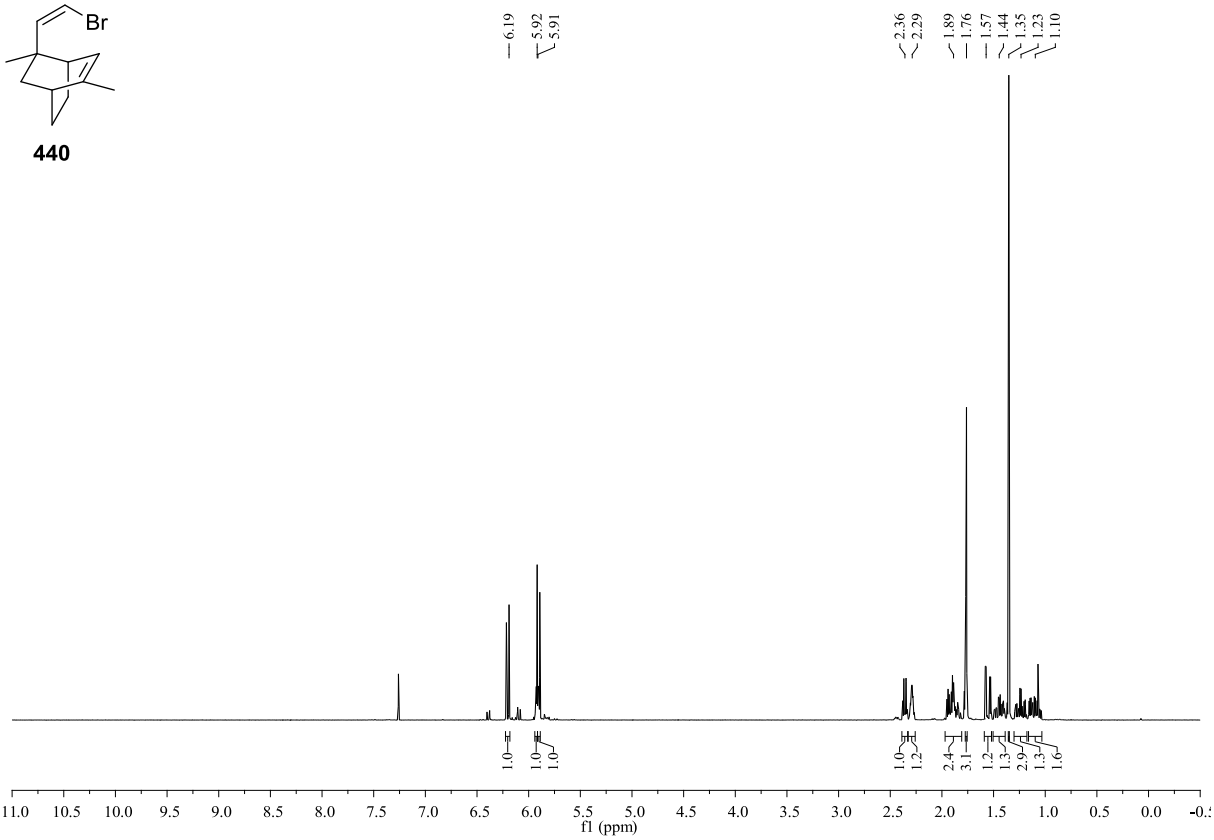
447 (^{1}H NMR, 600 MHz, $CDCl_3$)



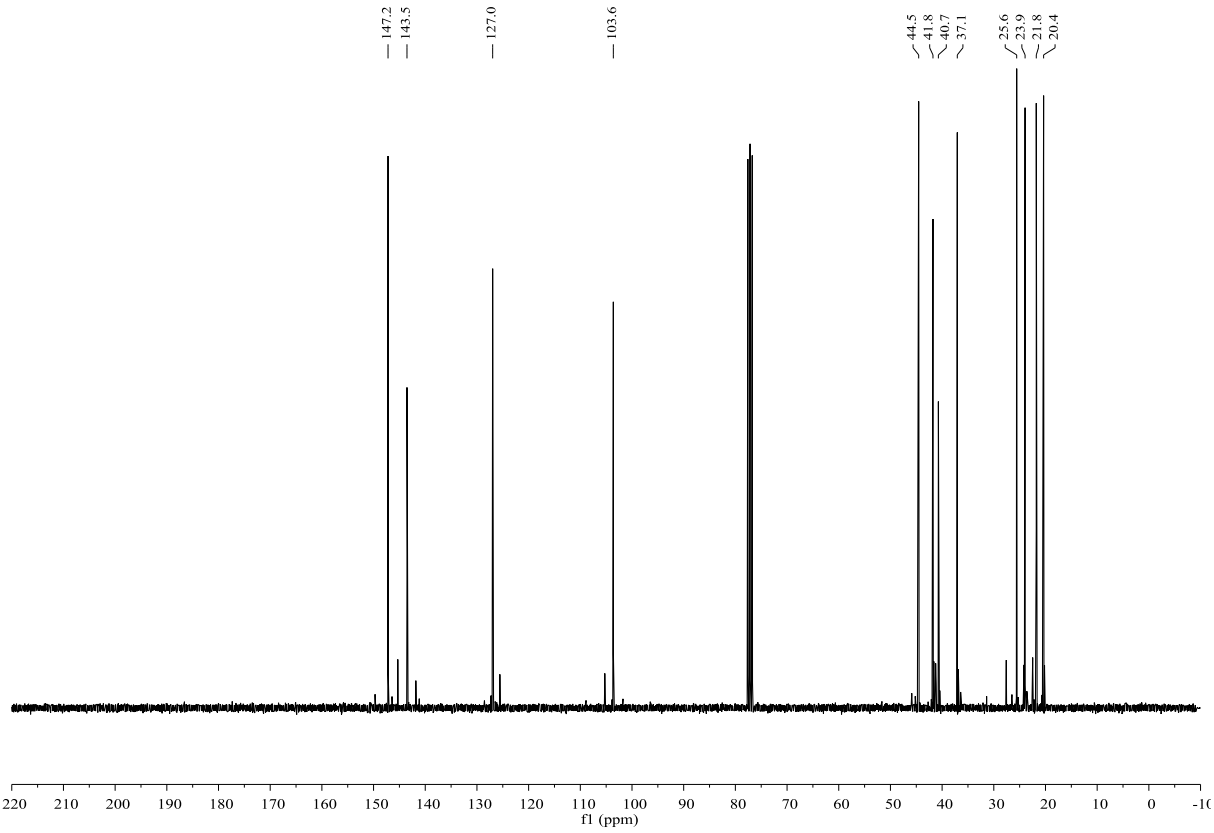
447 (^{13}C NMR, 150 MHz, $CDCl_3$)



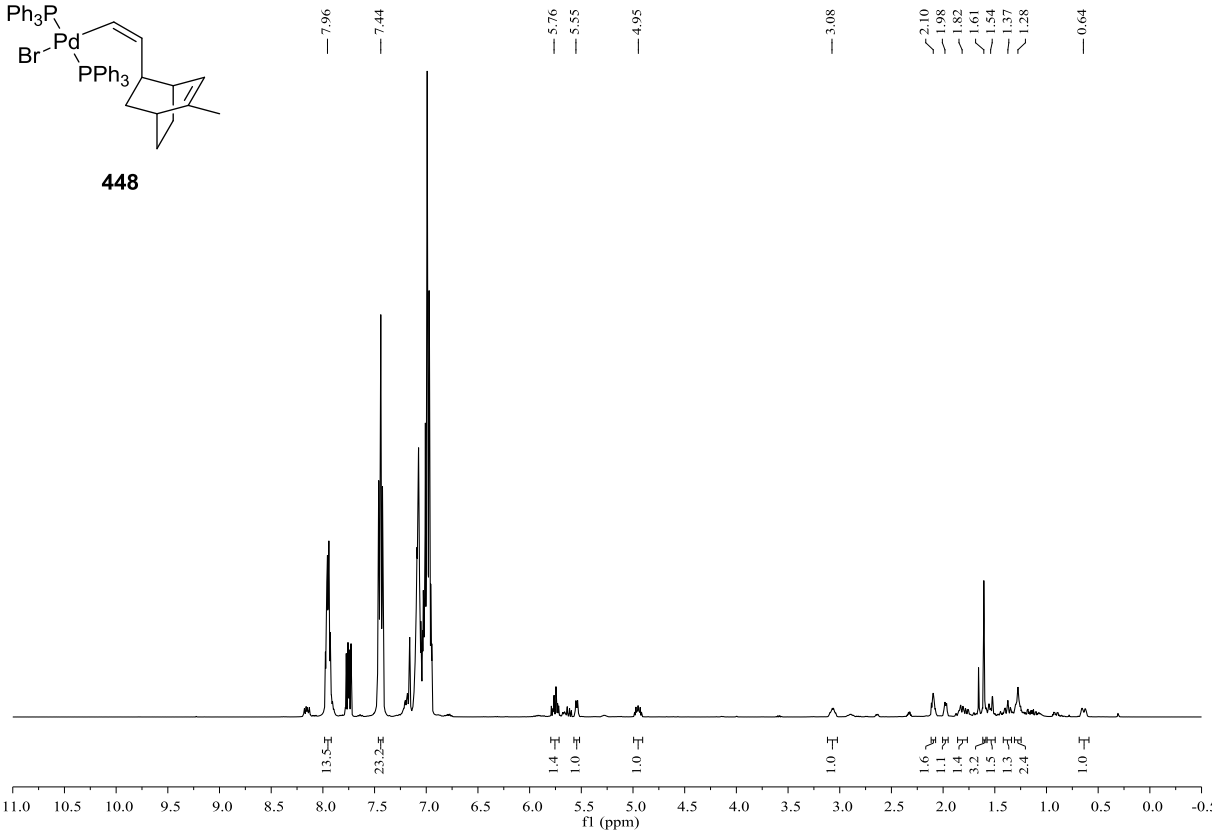
440 (^{1}H NMR, 300 MHz, $CDCl_3$)



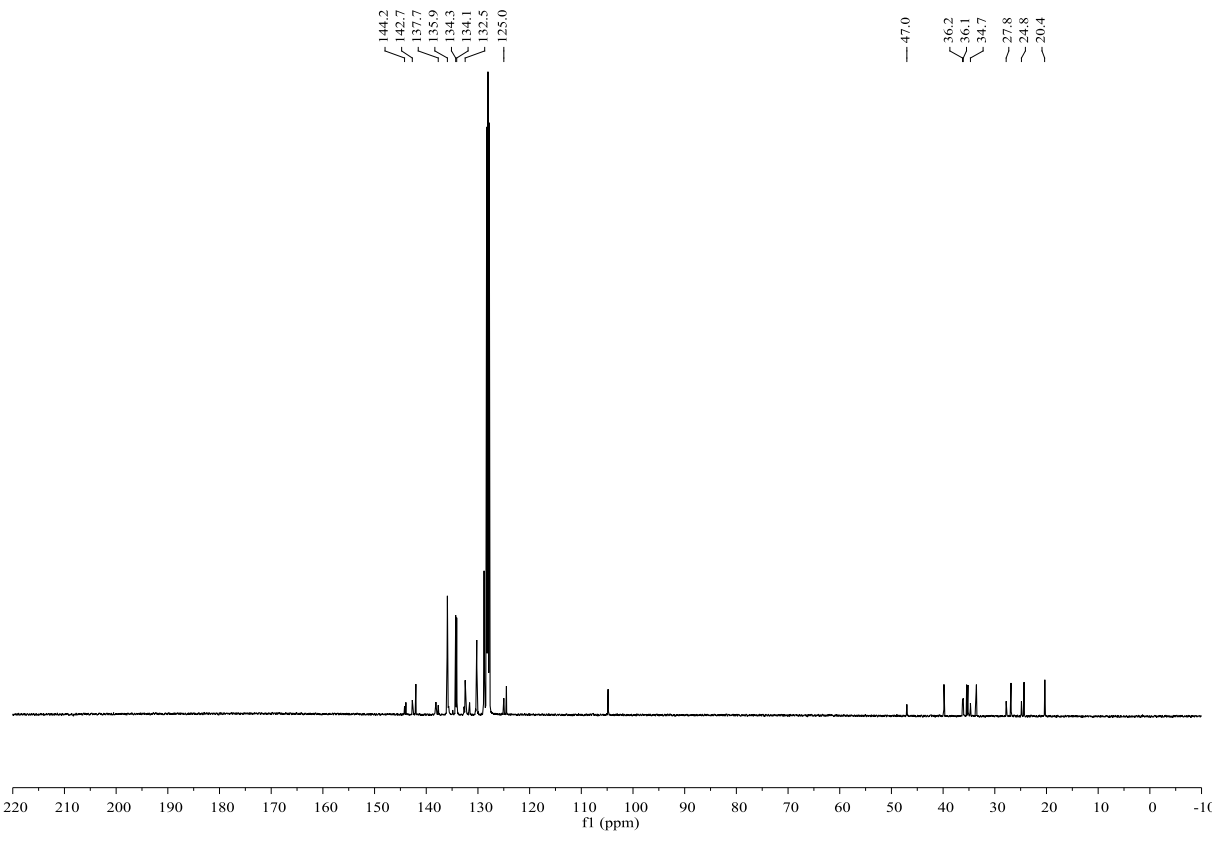
440 (^{13}C NMR, 75 MHz, $CDCl_3$)



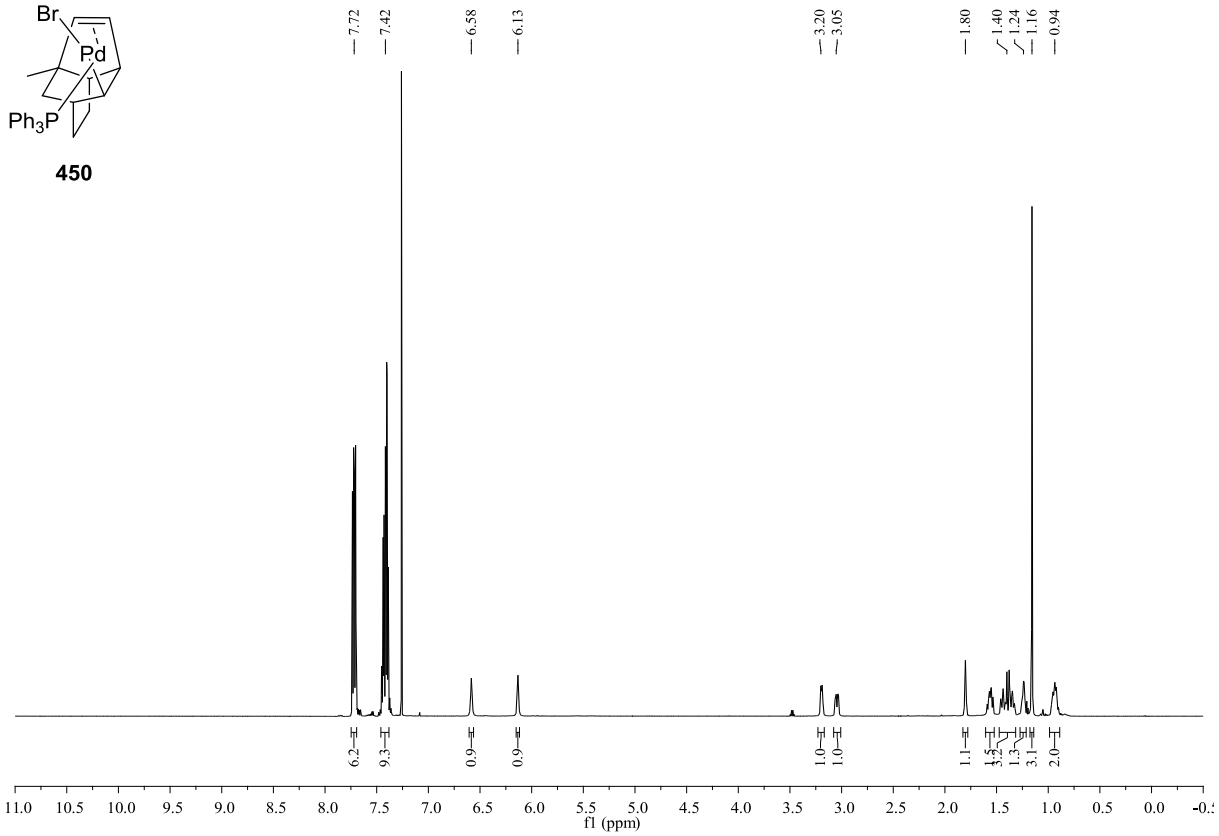
448 (^{1}H NMR, 400 MHz, C_6D_6)



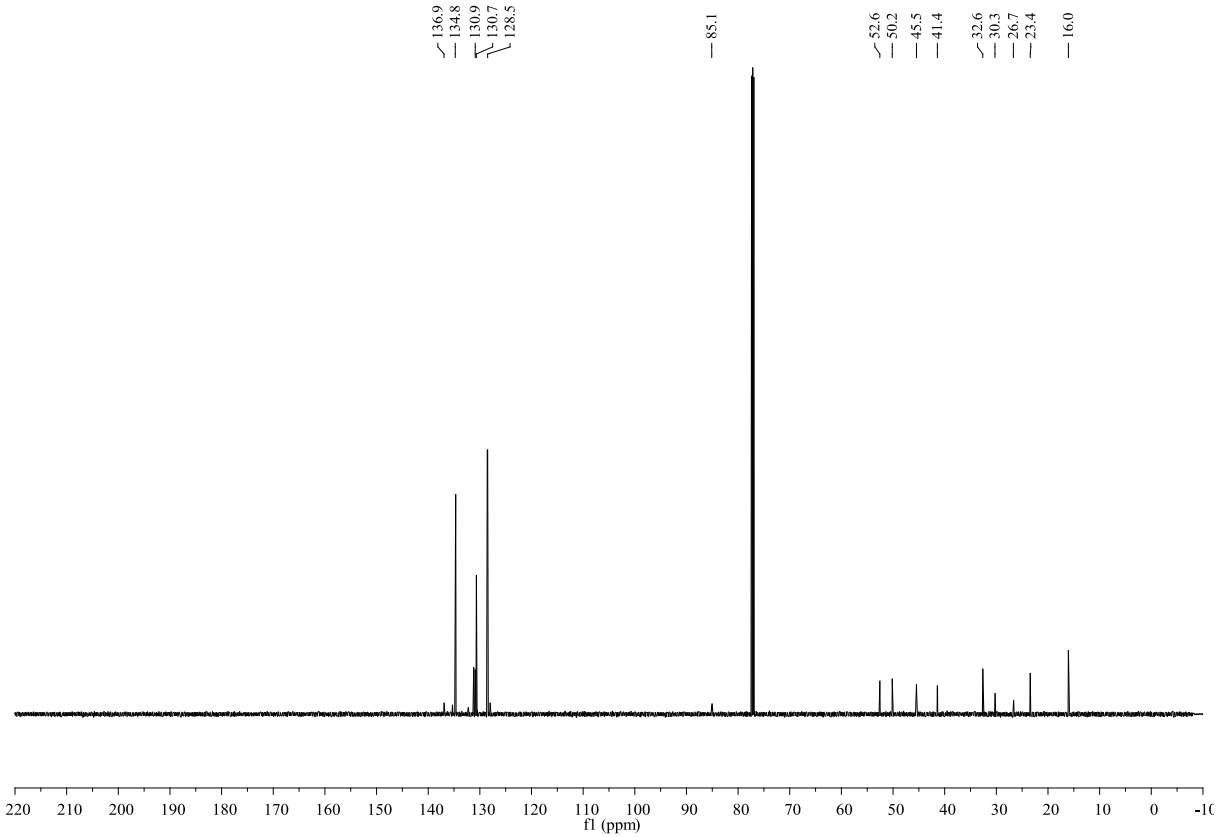
448 (^{13}C NMR, 100 MHz, C_6D_6)



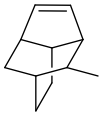
450 (^{1}H NMR, 600 MHz, $CDCl_3$)



450 (^{13}C NMR, 150 MHz, $CDCl_3$)

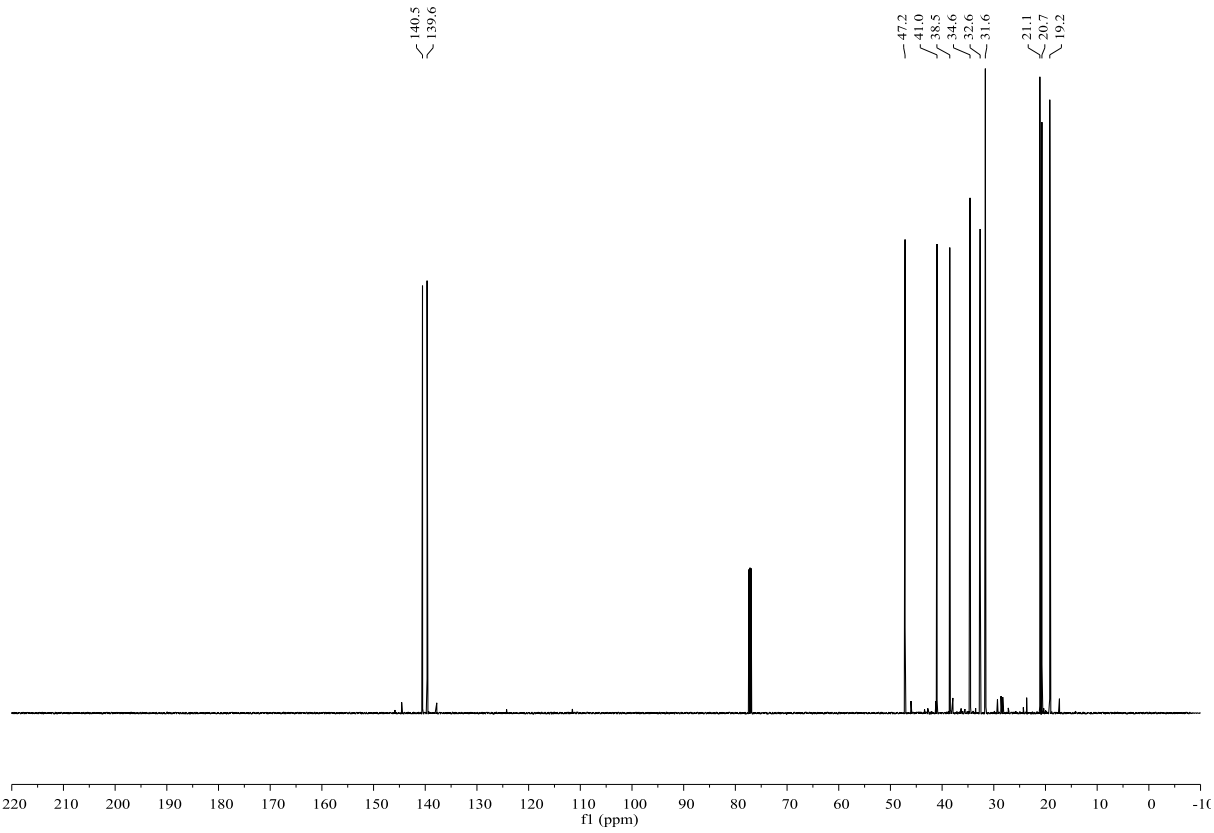


452 (^{1}H NMR, 600 MHz, $CDCl_3$)

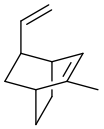


452

452 (^{13}C NMR, 150 MHz, $CDCl_3$)

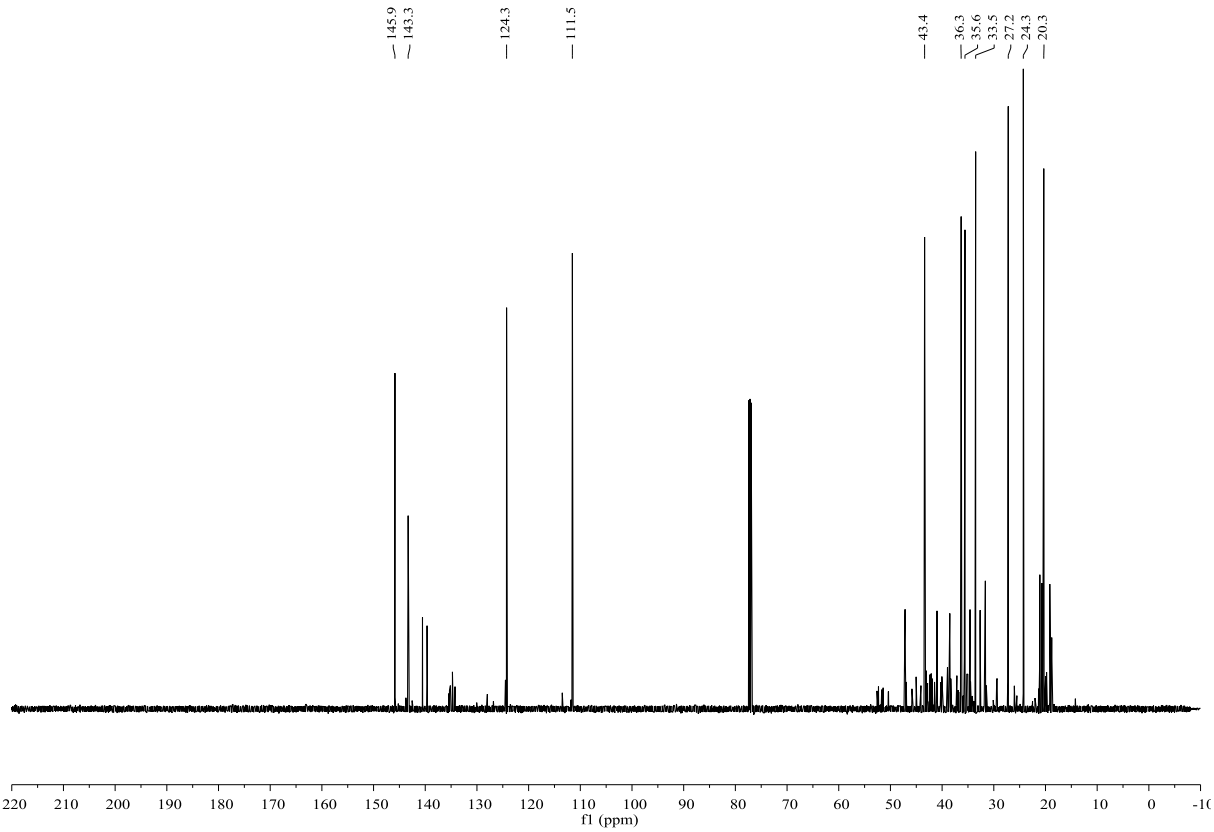


453 (^{1}H NMR, 600 MHz, $CDCl_3$)

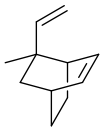


453

453 (^{13}C NMR, 150 MHz, $CDCl_3$)

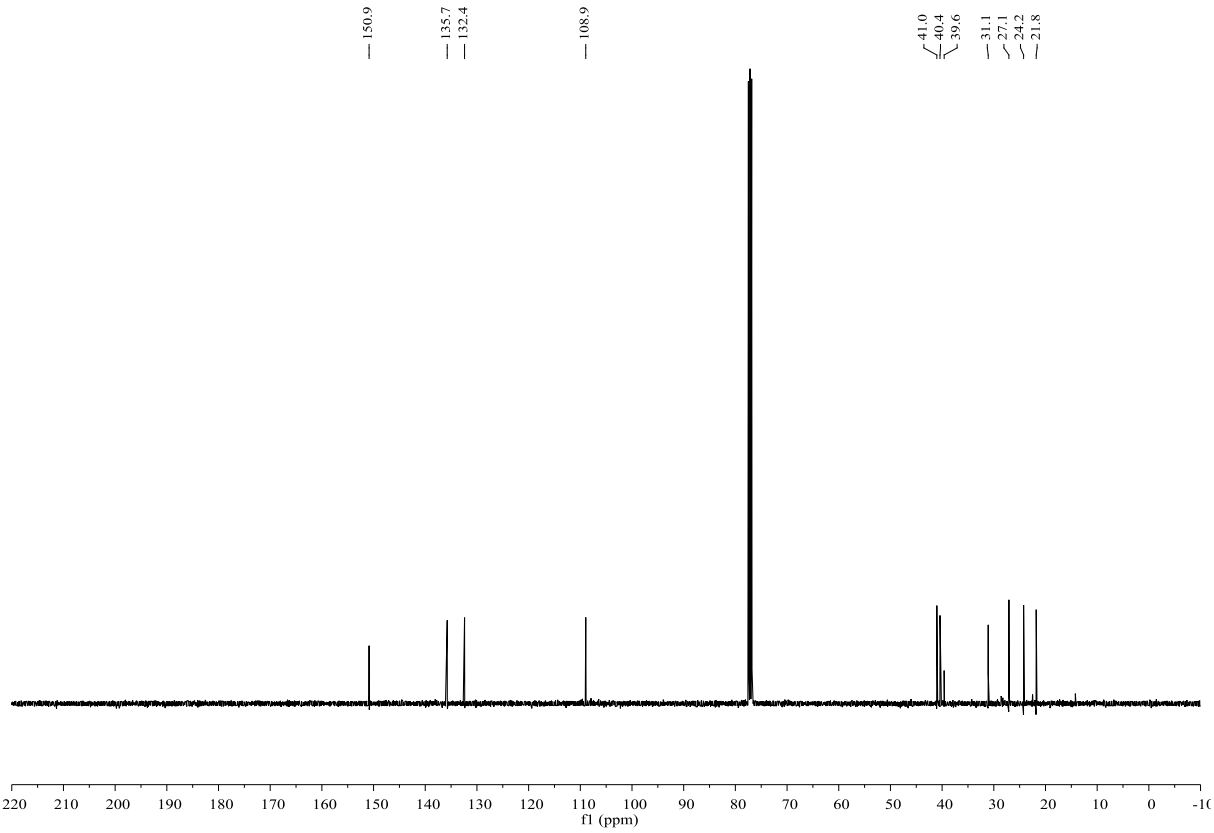


454 (^{1}H NMR, 400 MHz, $CDCl_3$)

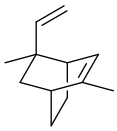


454

454 (^{13}C NMR, 100 MHz, $CDCl_3$)

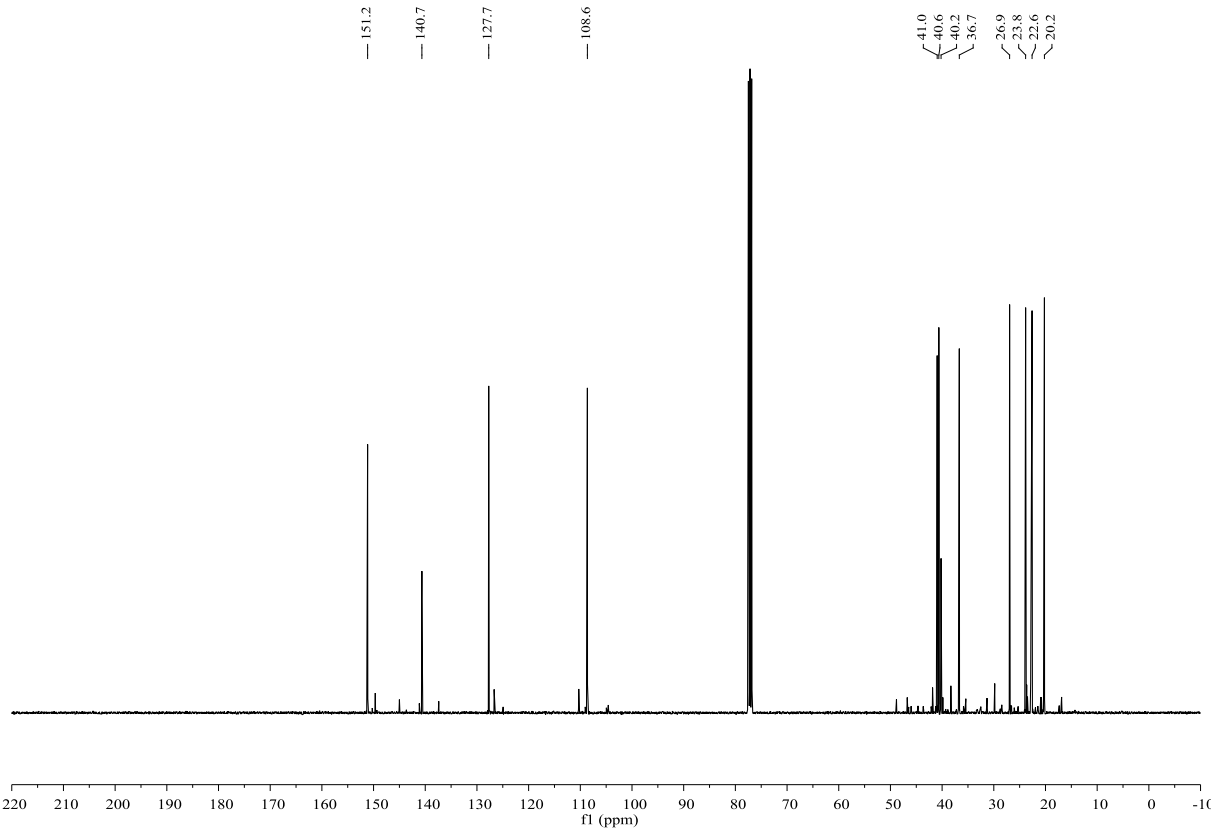


455 (^{1}H NMR, 400 MHz, $CDCl_3$)

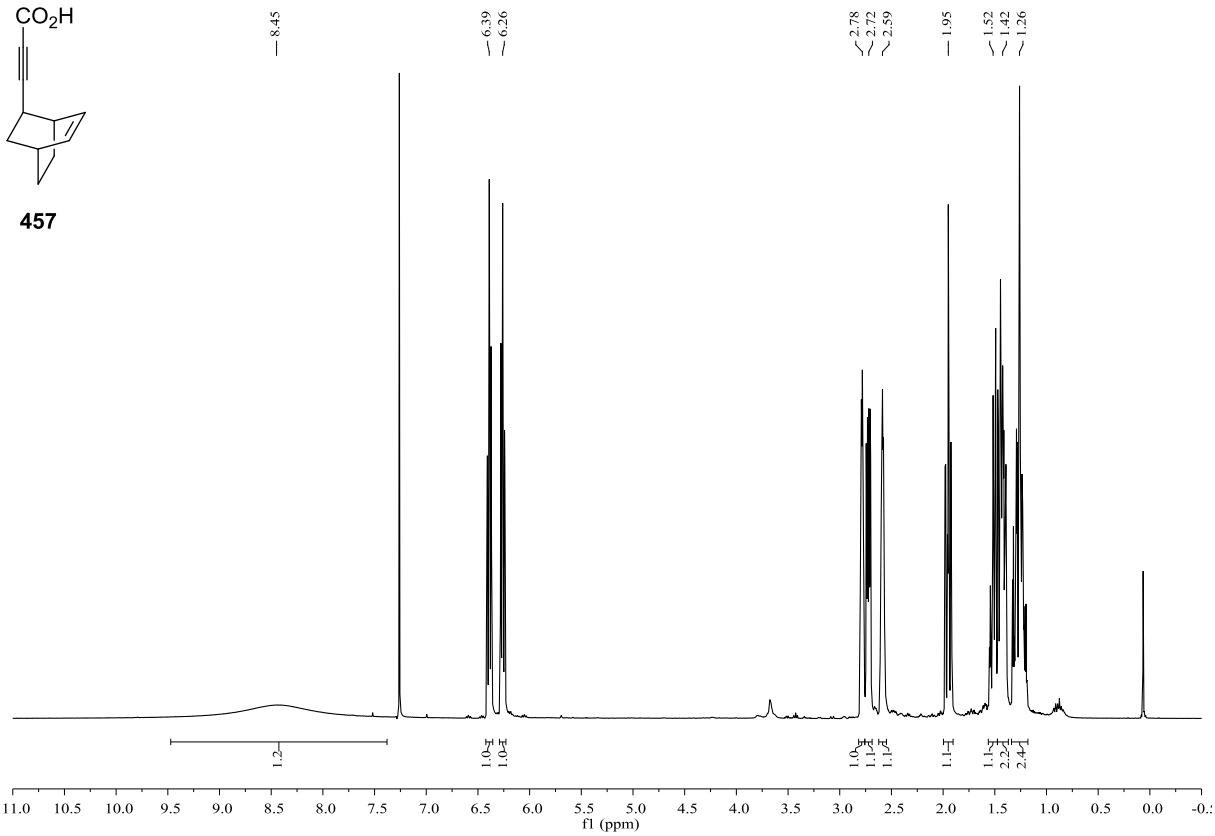


455

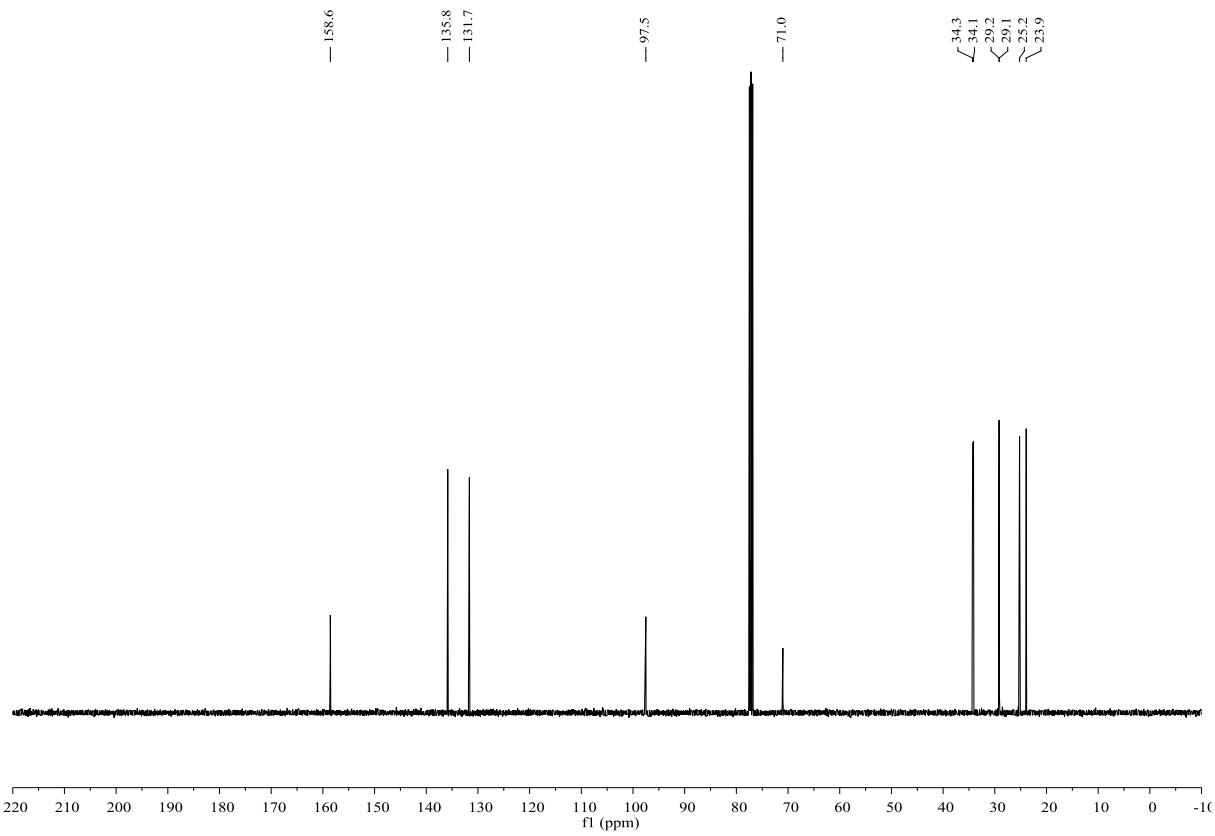
455 (^{13}C NMR, 100 MHz, $CDCl_3$)



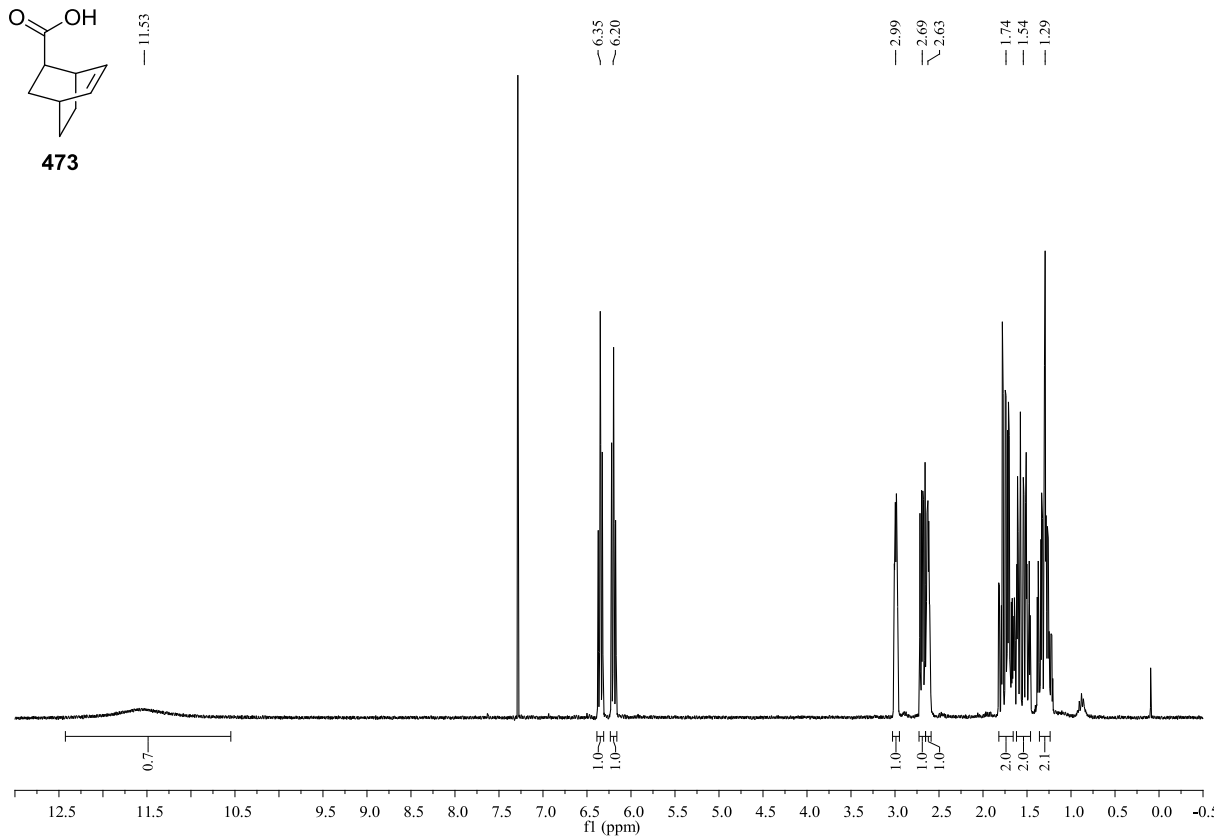
457 (^{1}H NMR, 400 MHz, $CDCl_3$)



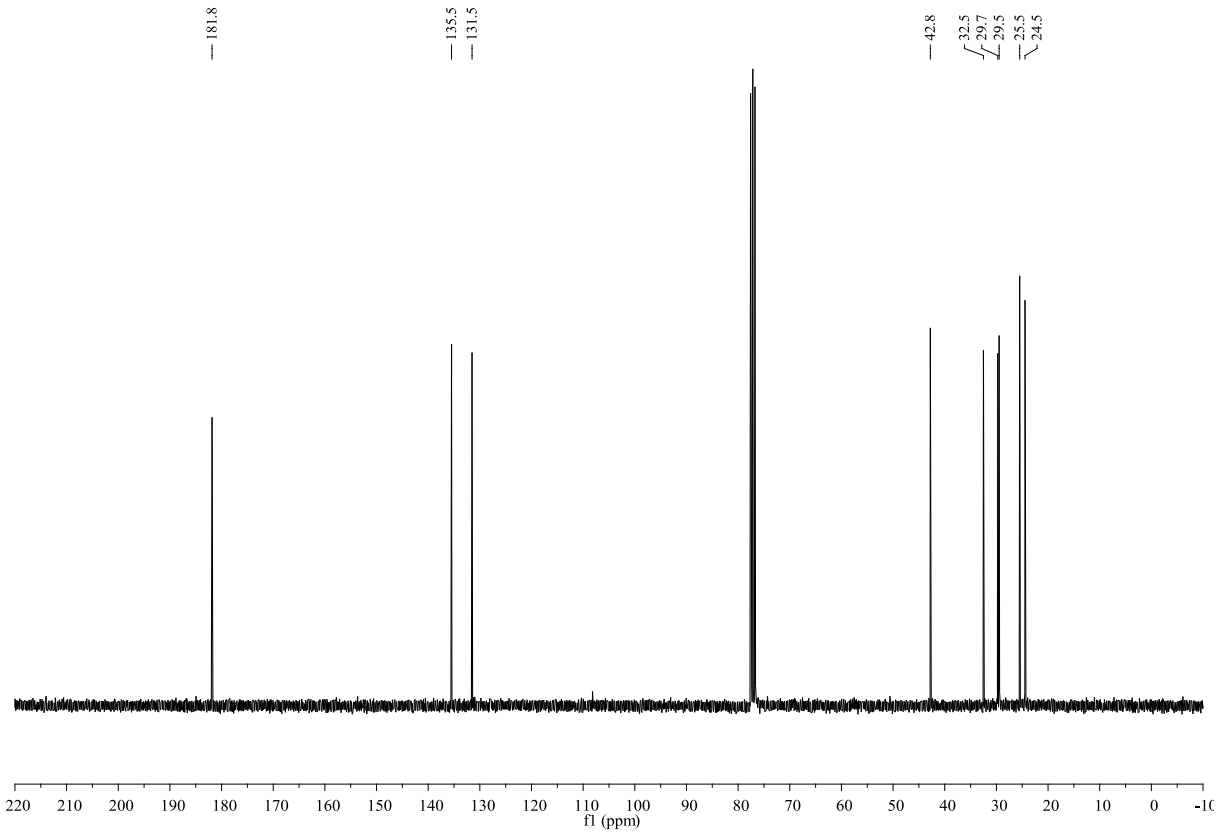
457 (^{13}C NMR, 100 MHz, $CDCl_3$)



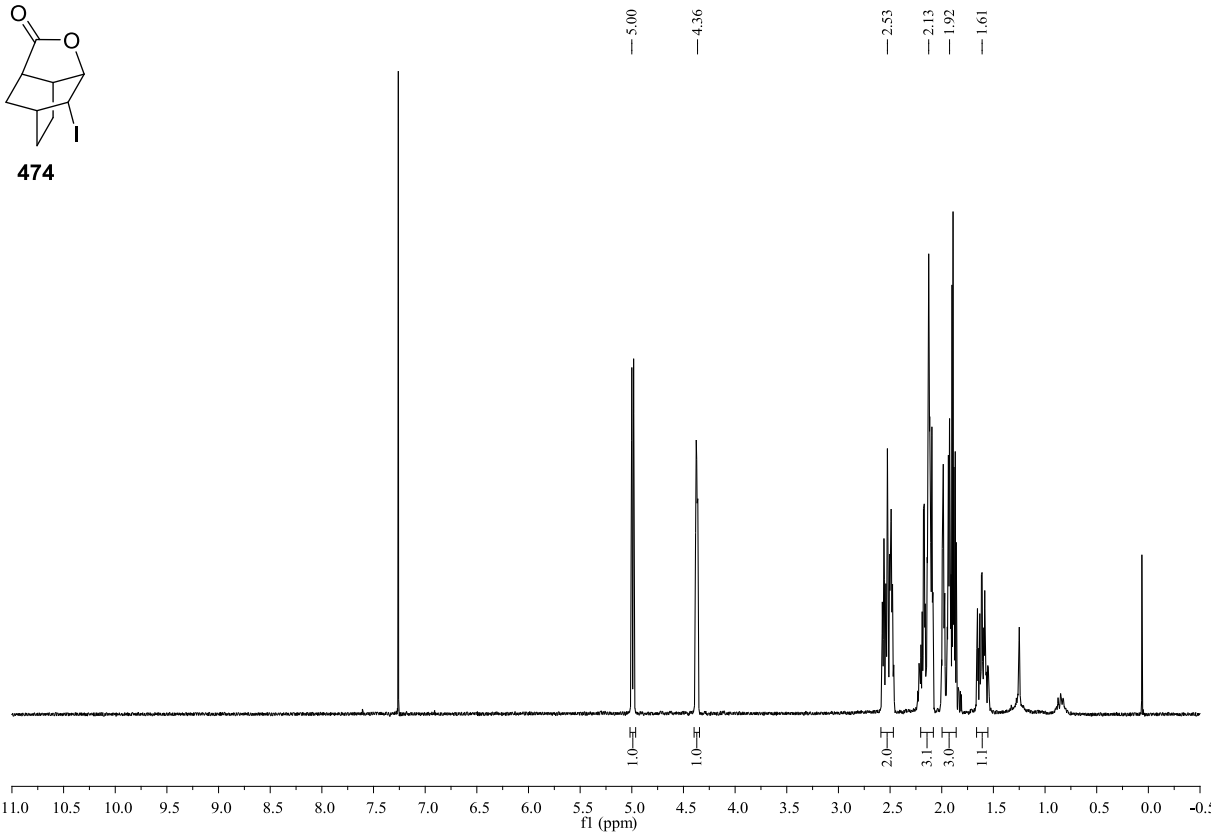
473 (^{1}H NMR, 300 MHz, $CDCl_3$)



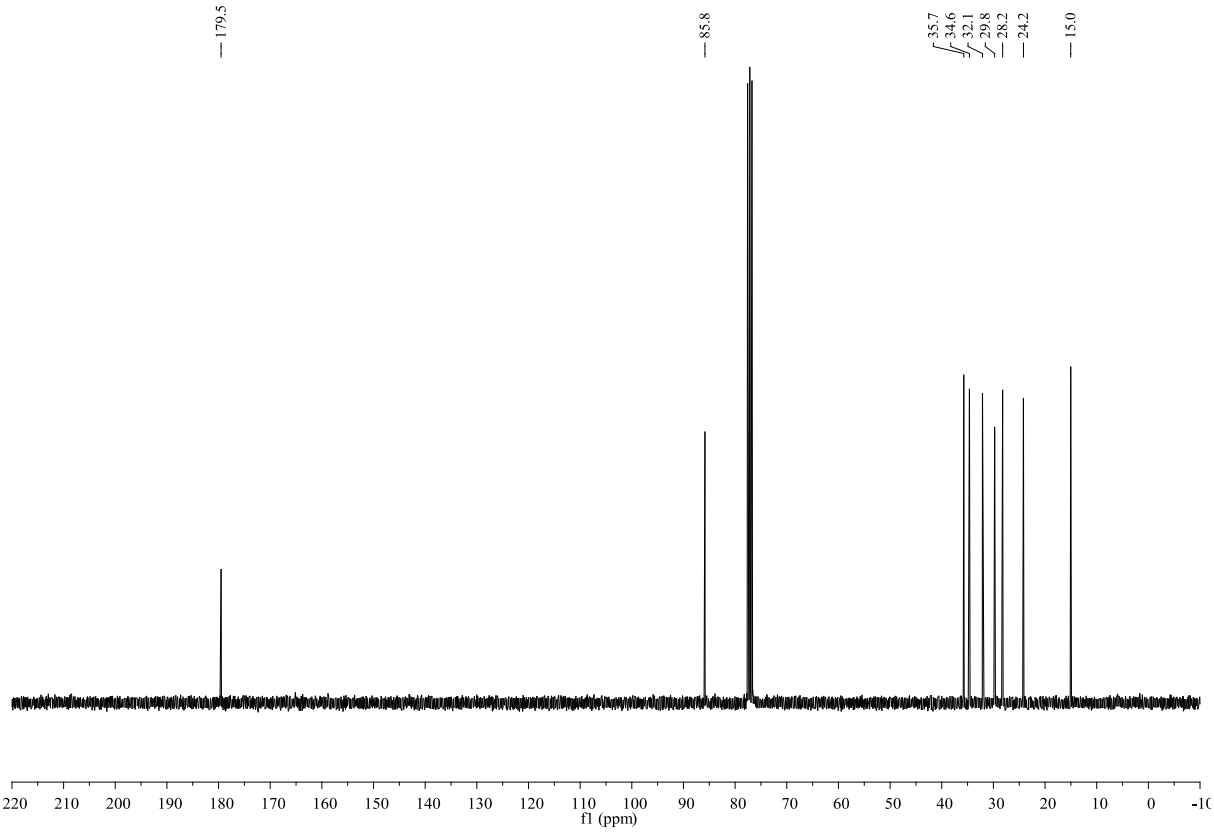
473 (^{13}C NMR, 75 MHz, $CDCl_3$)



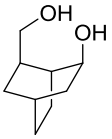
474 (^{1}H NMR, 300 MHz, $CDCl_3$)



474 (^{13}C NMR, 75 MHz, $CDCl_3$)

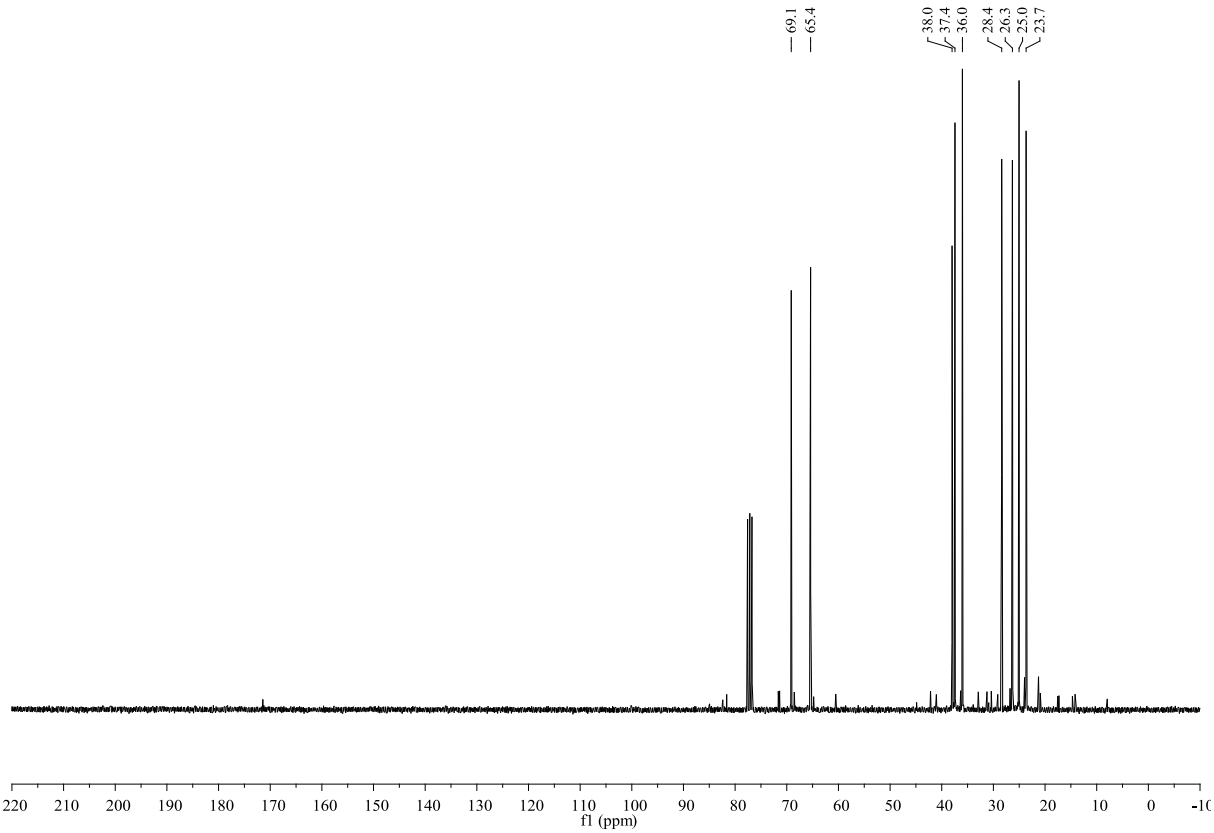


475 (^{1}H NMR, 300 MHz, $CDCl_3$)

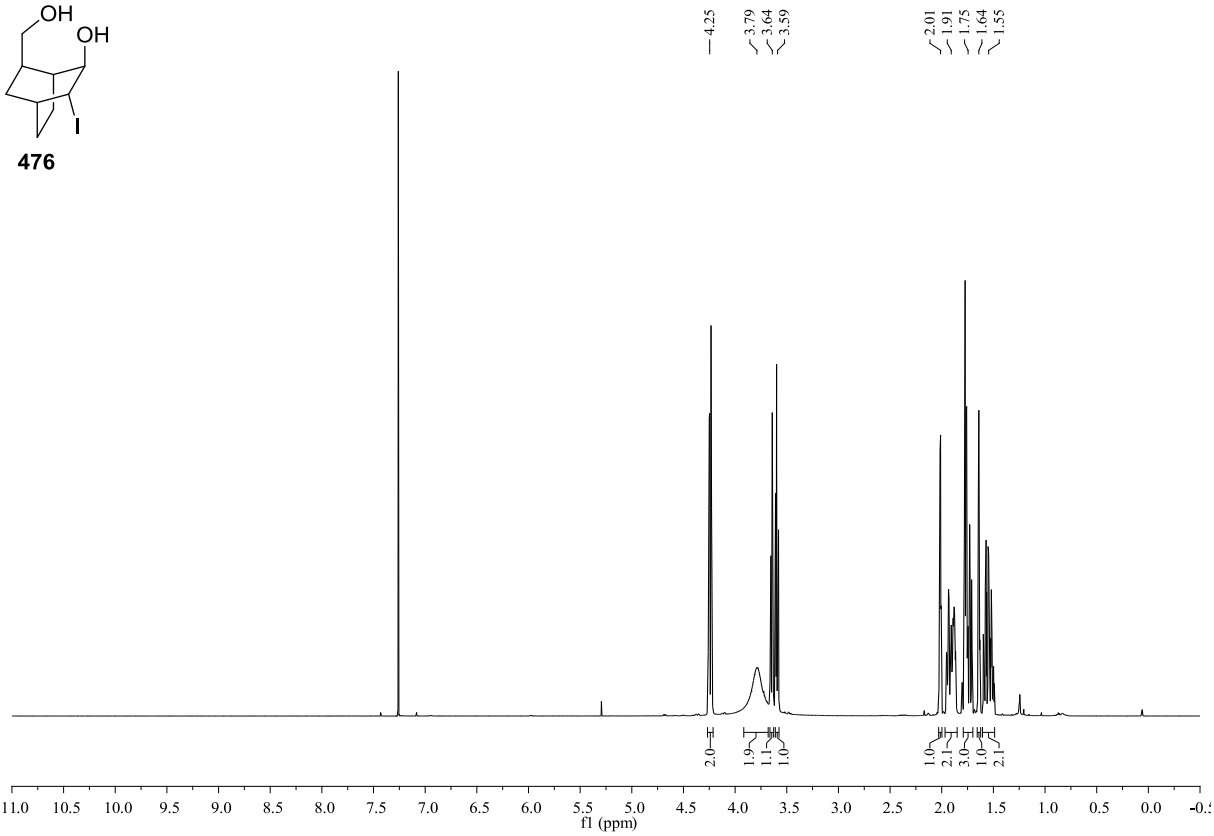


475

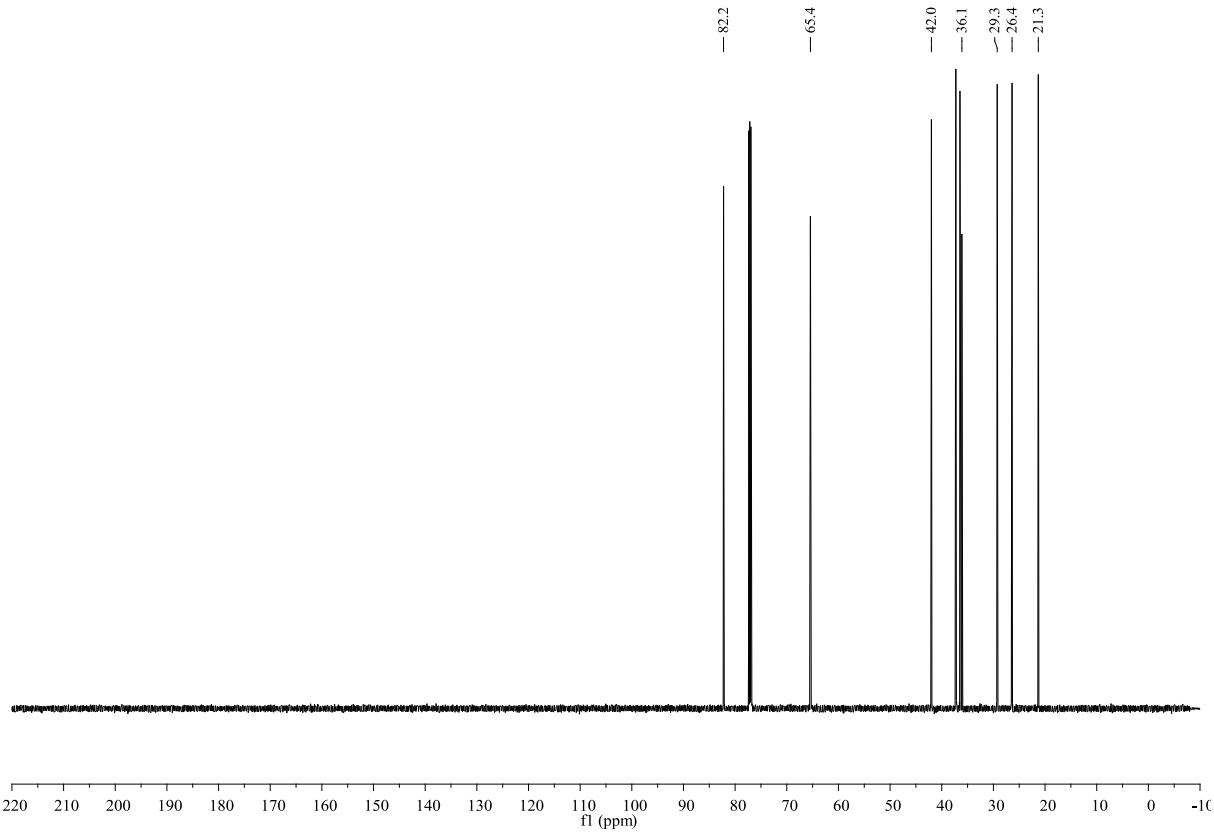
475 (^{13}C NMR, 75 MHz, $CDCl_3$)



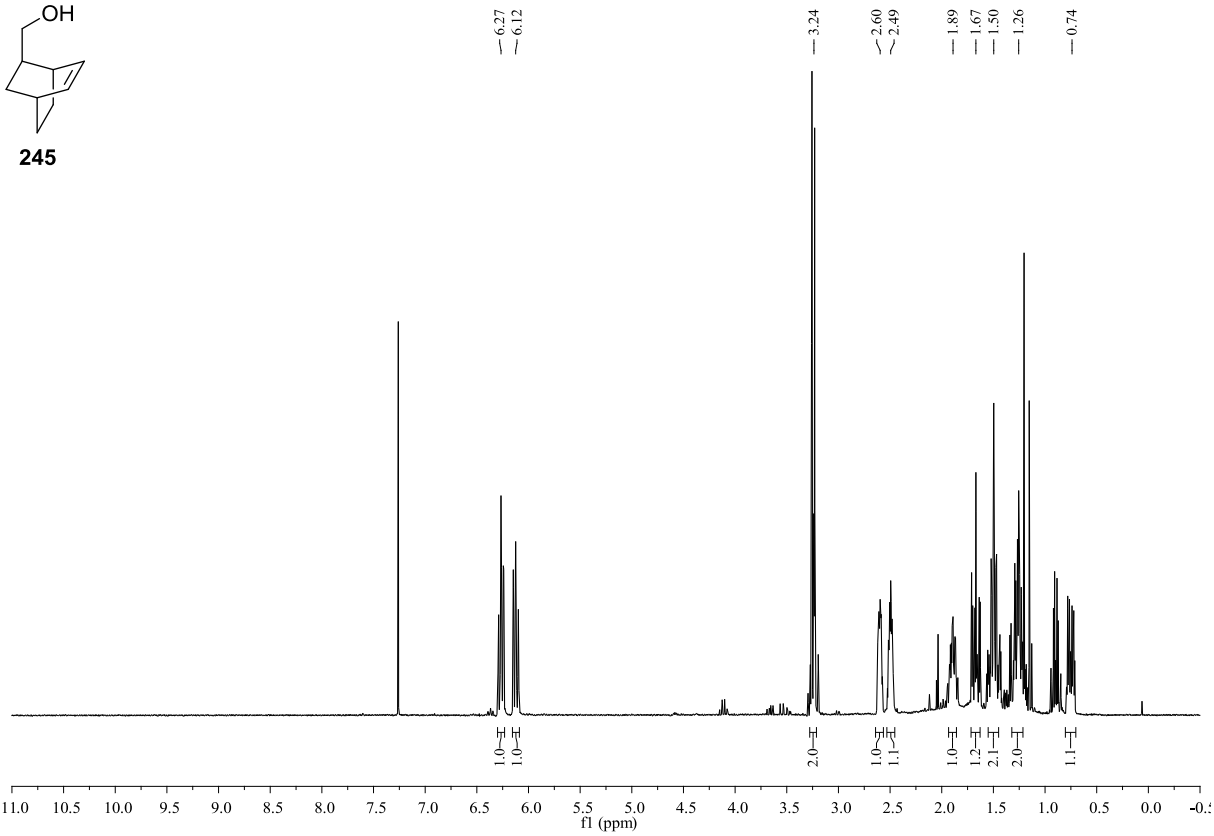
476 (^{1}H NMR, 600 MHz, $CDCl_3$)



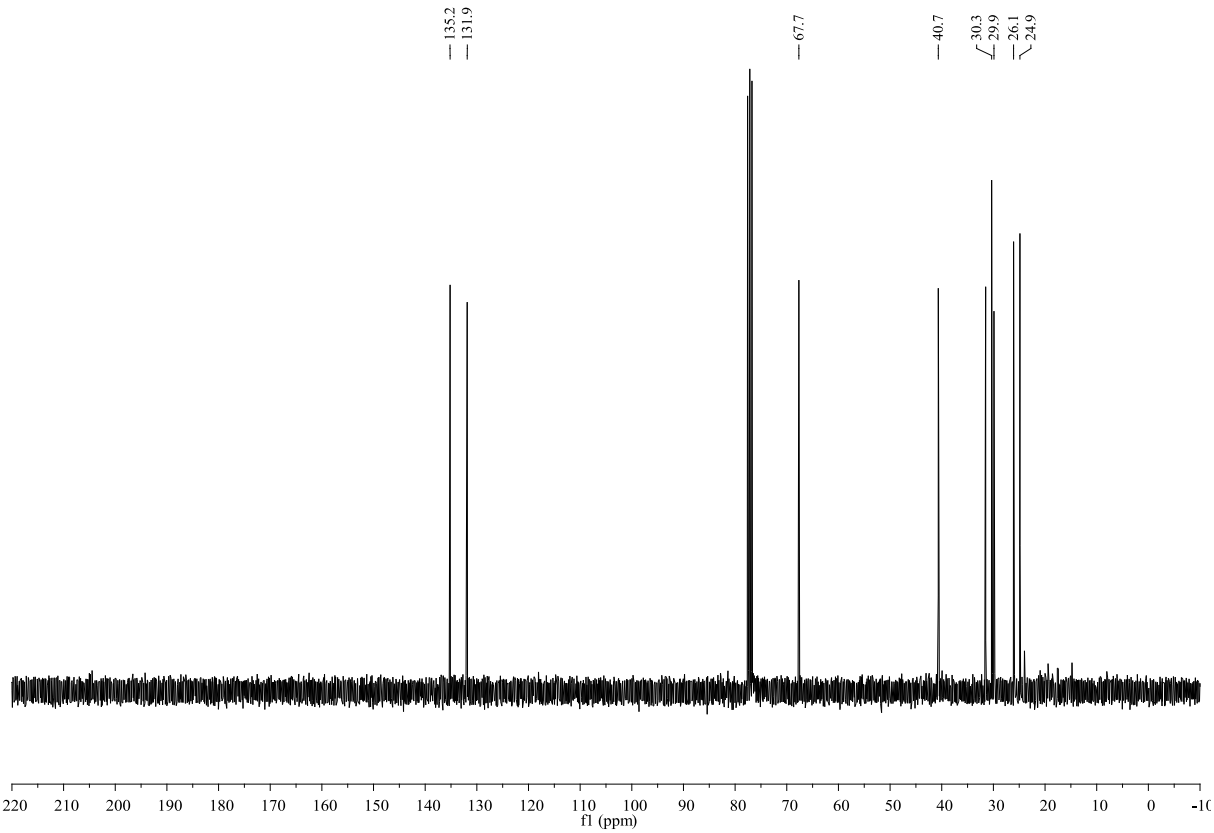
476 (^{13}C NMR, 150 MHz, $CDCl_3$)



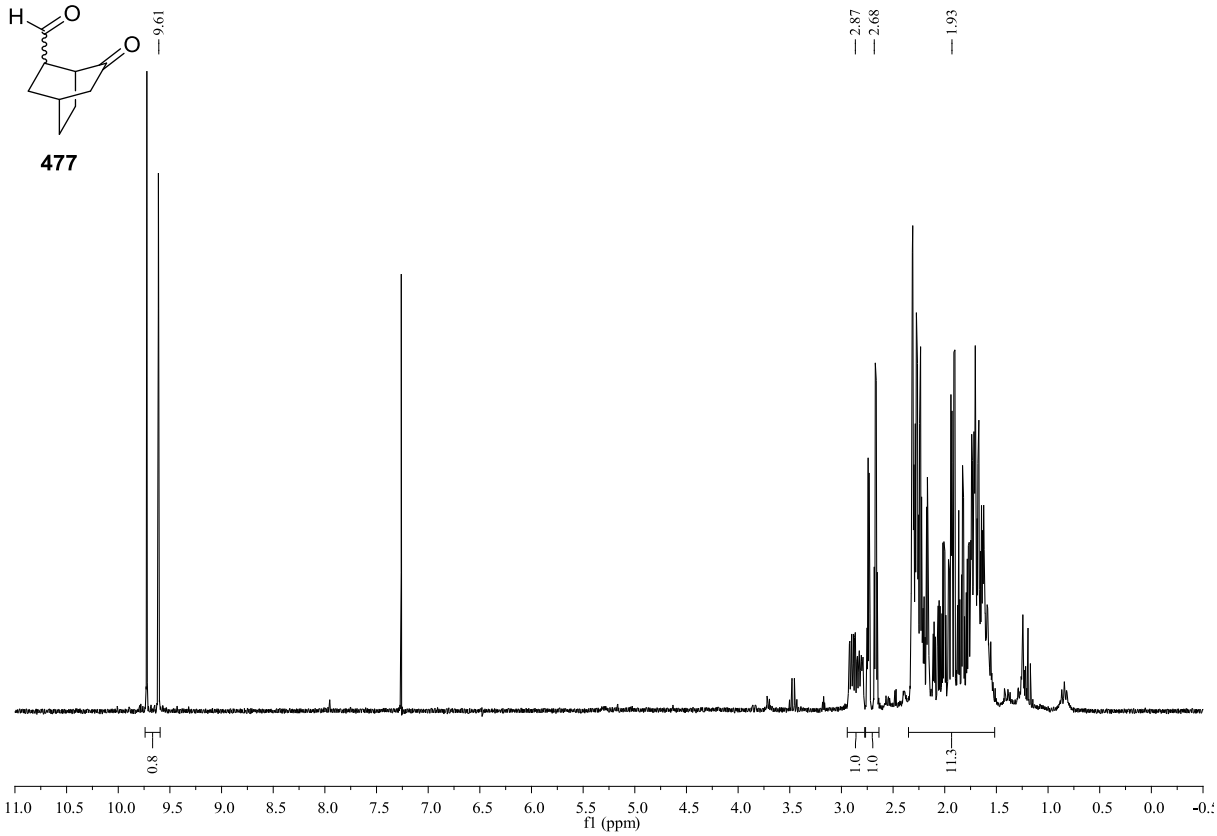
245 (^{1}H NMR, 300 MHz, $CDCl_3$)



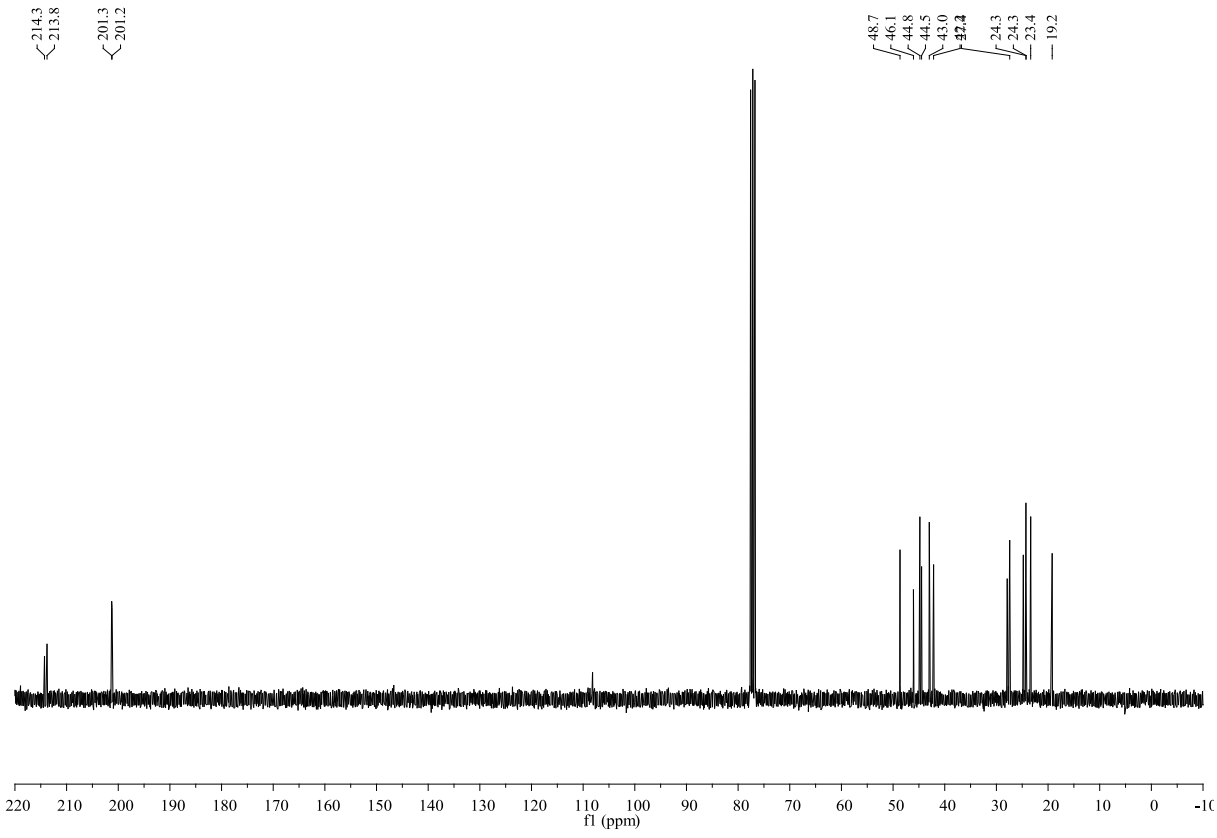
245 (^{13}C NMR, 75 MHz, $CDCl_3$)



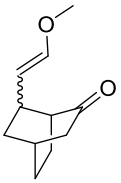
477 (^{1}H NMR, 300 MHz, $CDCl_3$)



477 (^{13}C NMR, 75 MHz, $CDCl_3$)

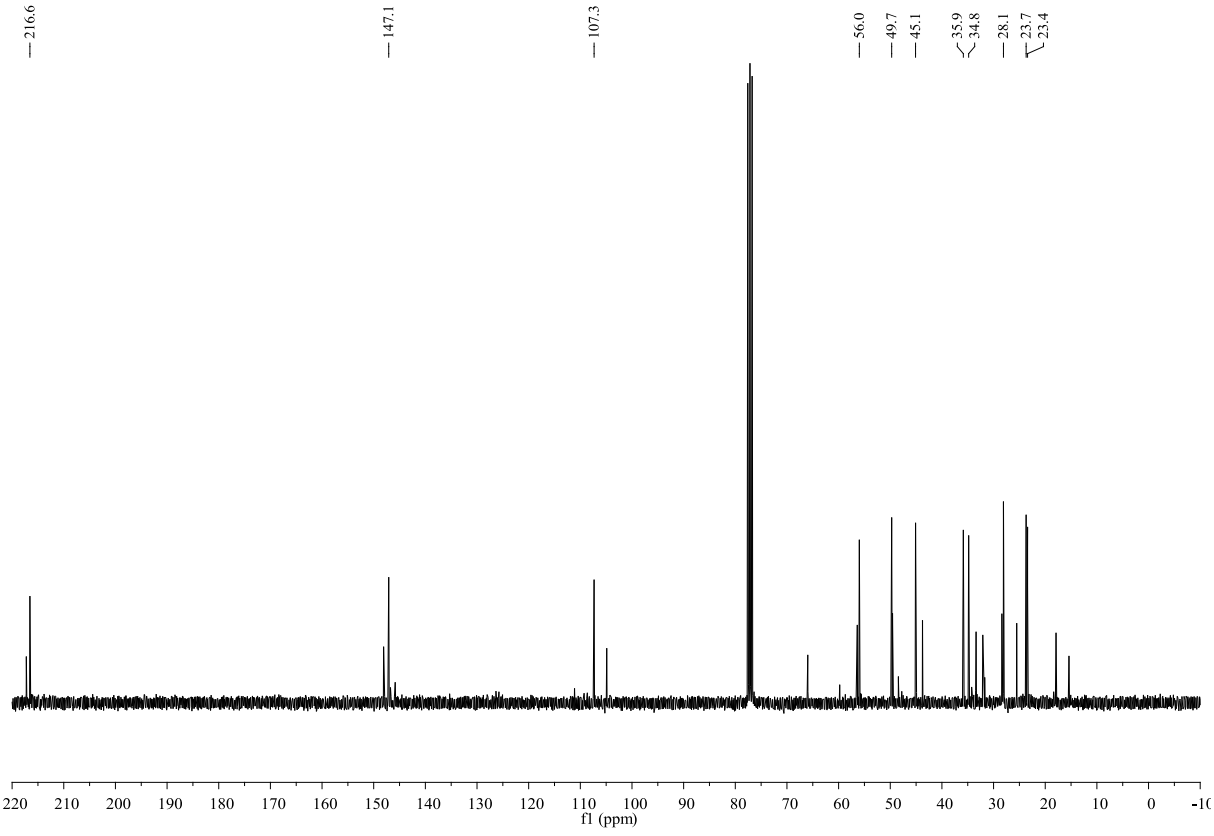


472 (^{1}H NMR, 300 MHz, $CDCl_3$)

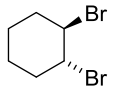


472

472 (^{13}C NMR, 75 MHz, $CDCl_3$)

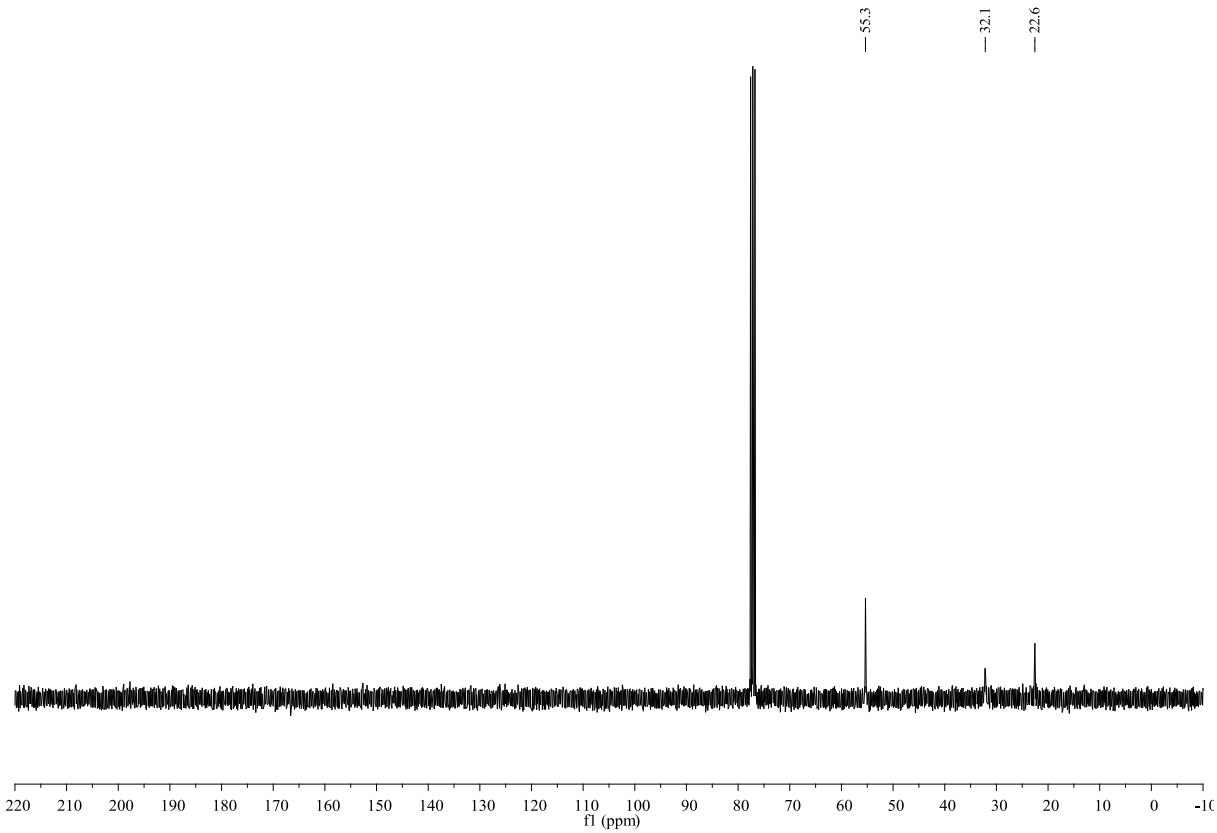


480 (^{1}H NMR, 300 MHz, $CDCl_3$)

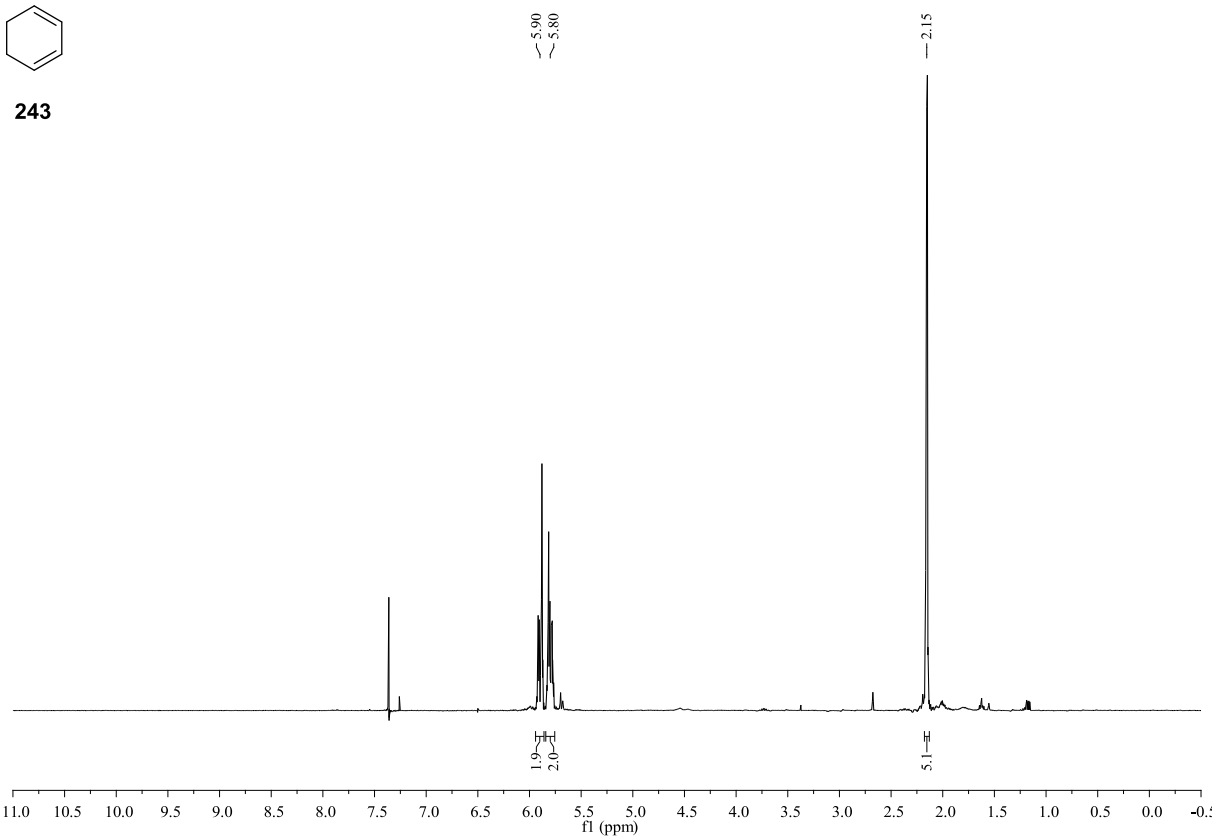


480

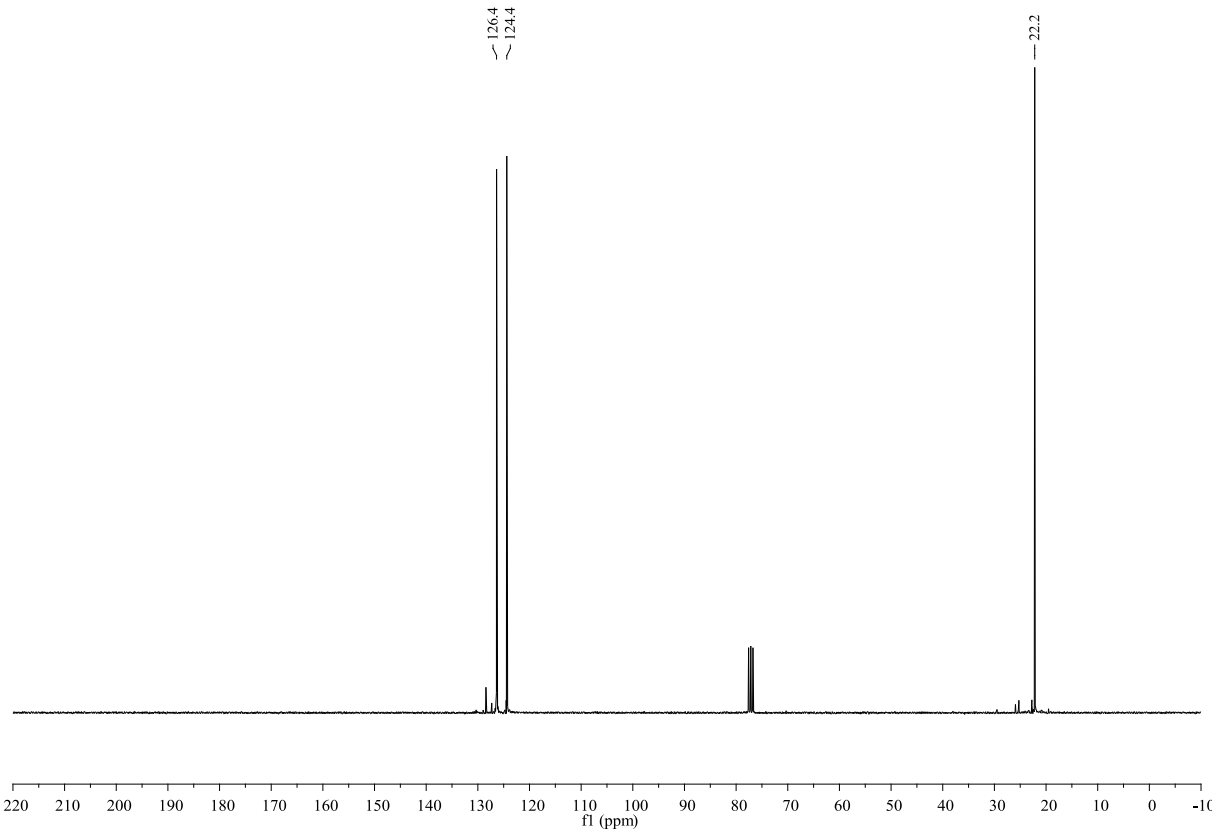
480 (^{13}C NMR, 75 MHz, $CDCl_3$)



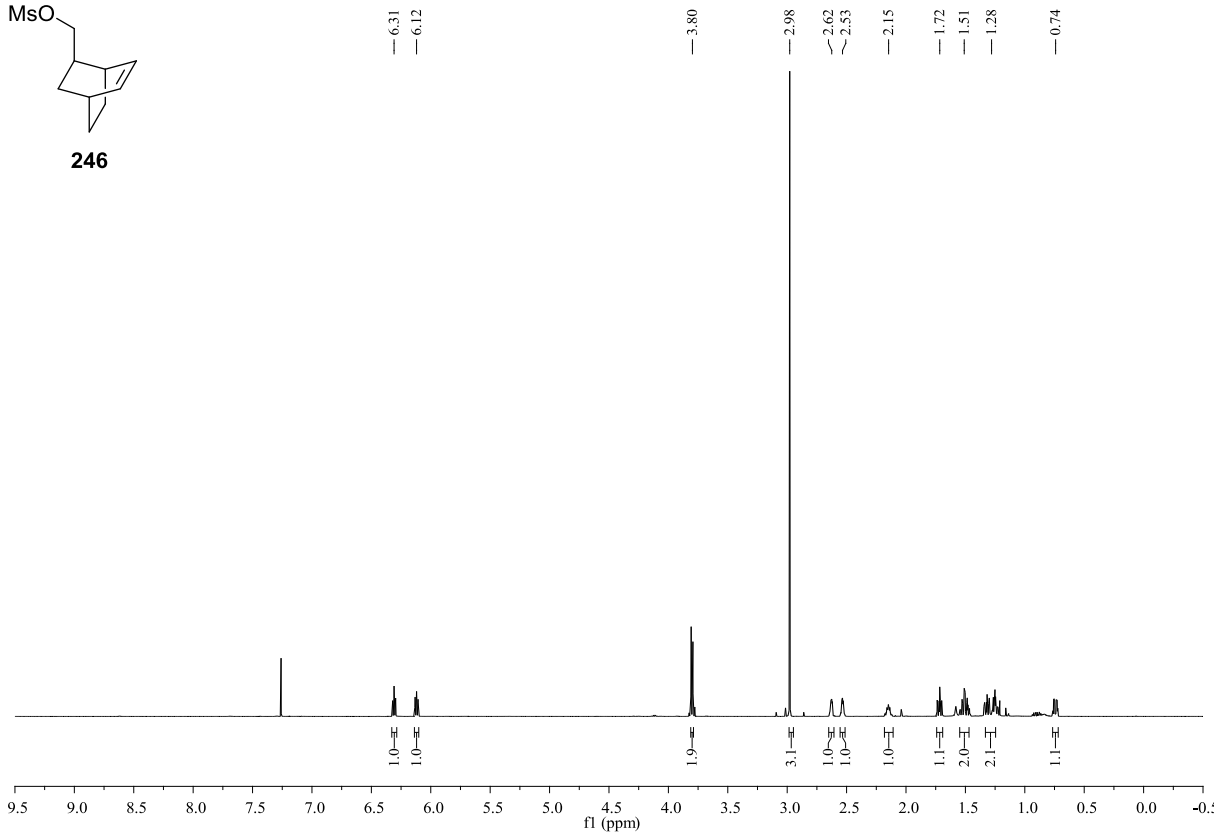
243 (^{1}H NMR, 300 MHz, $CDCl_3$)



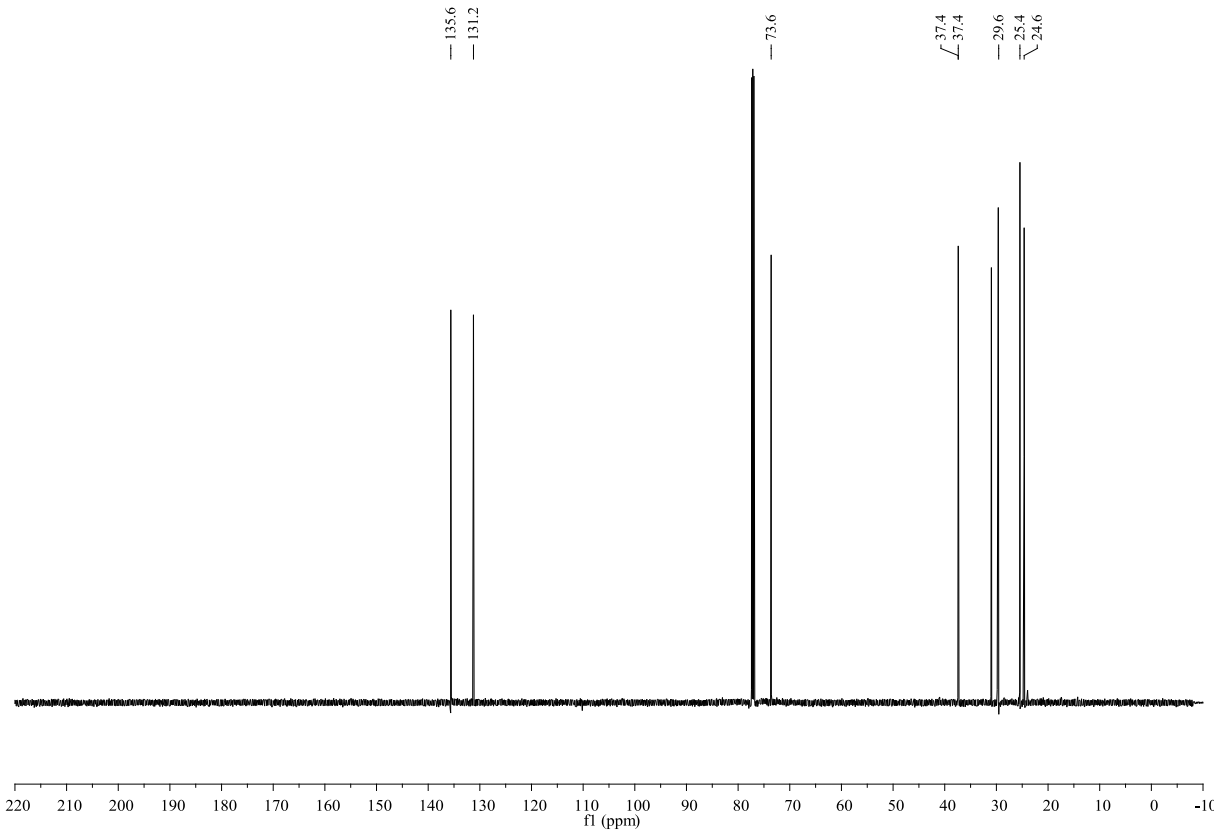
243 (^{13}C NMR, 75 MHz, $CDCl_3$)



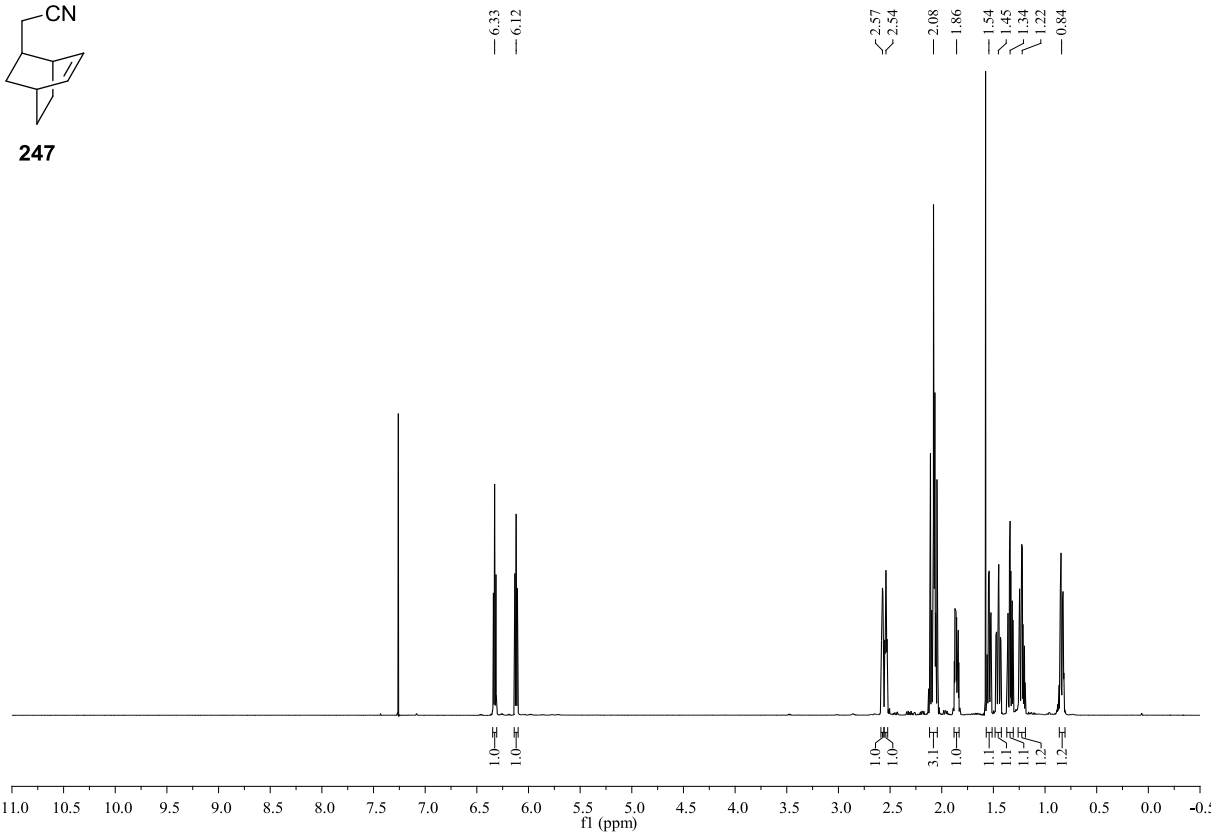
246 (^{1}H NMR, 600 MHz, $CDCl_3$)



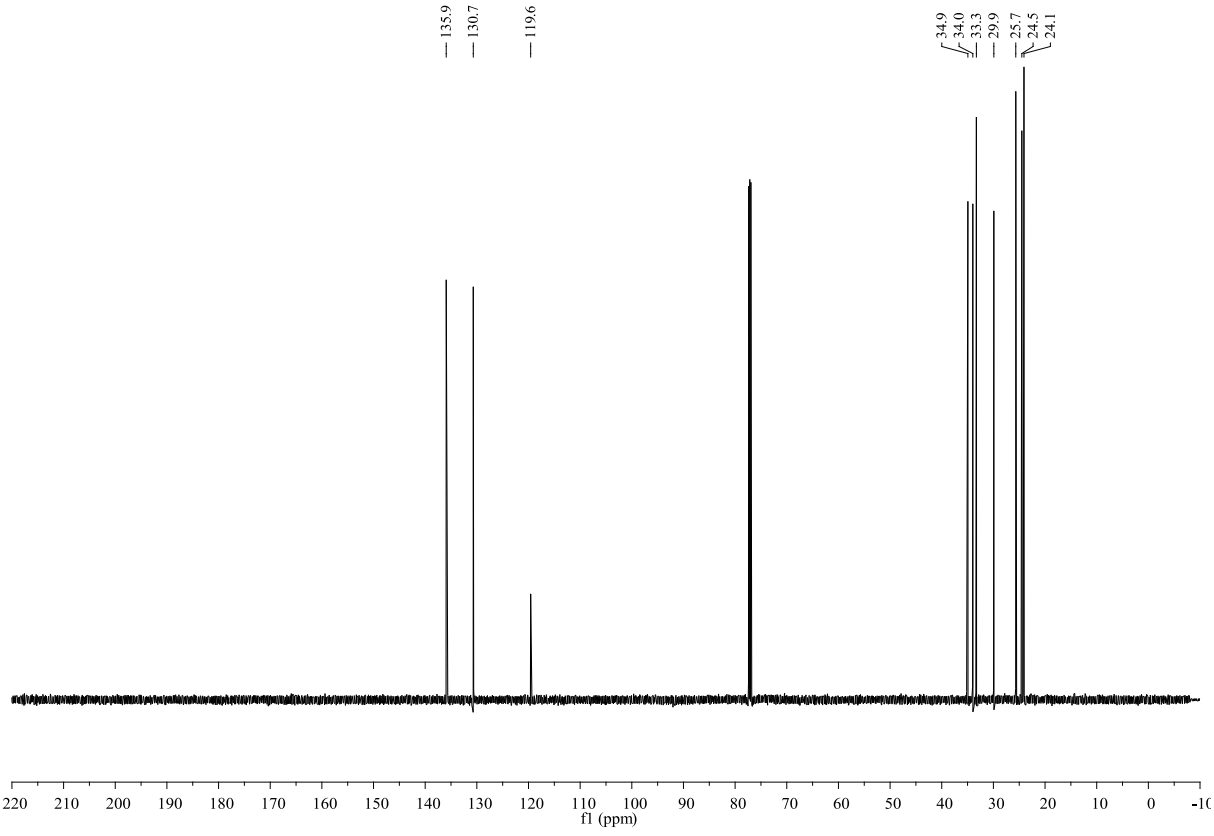
246 (^{13}C NMR, 150 MHz, $CDCl_3$)



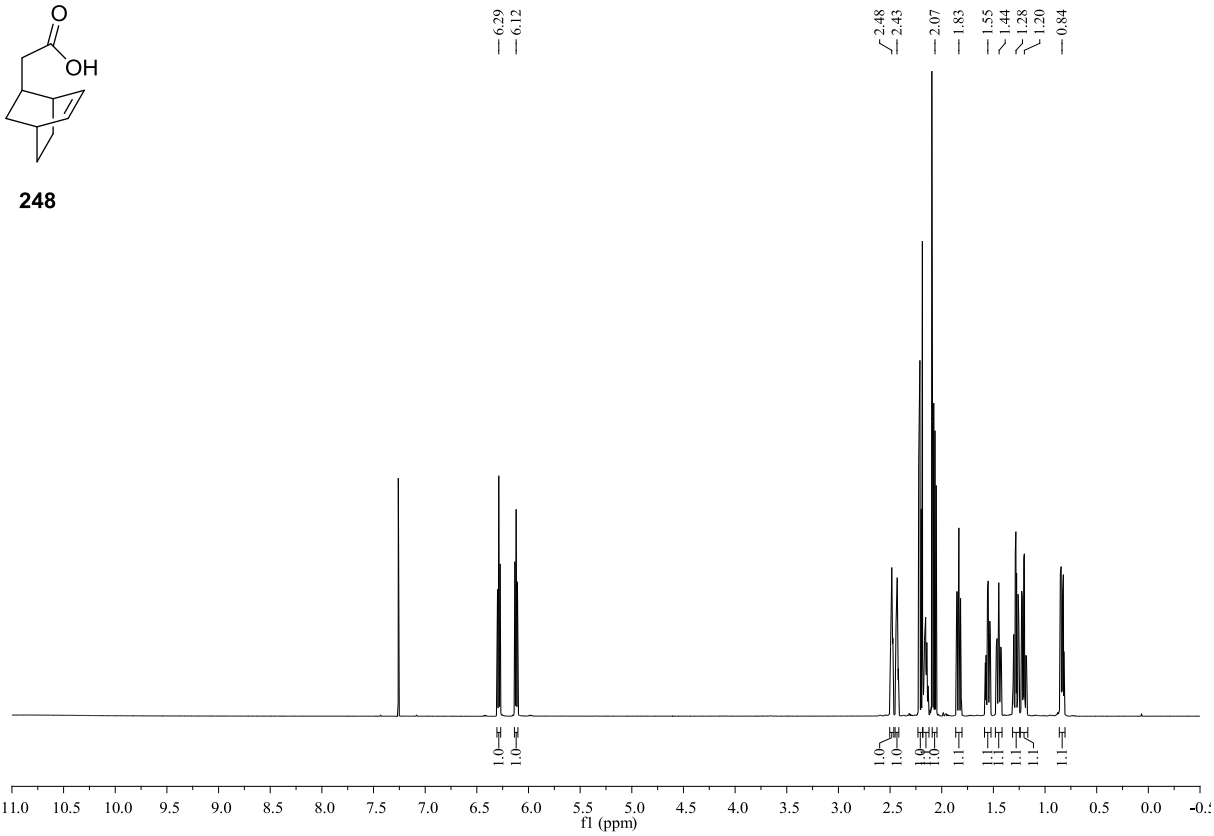
247 (^{1}H NMR, 600 MHz, $CDCl_3$)



247 (^{13}C NMR, 150 MHz, $CDCl_3$)

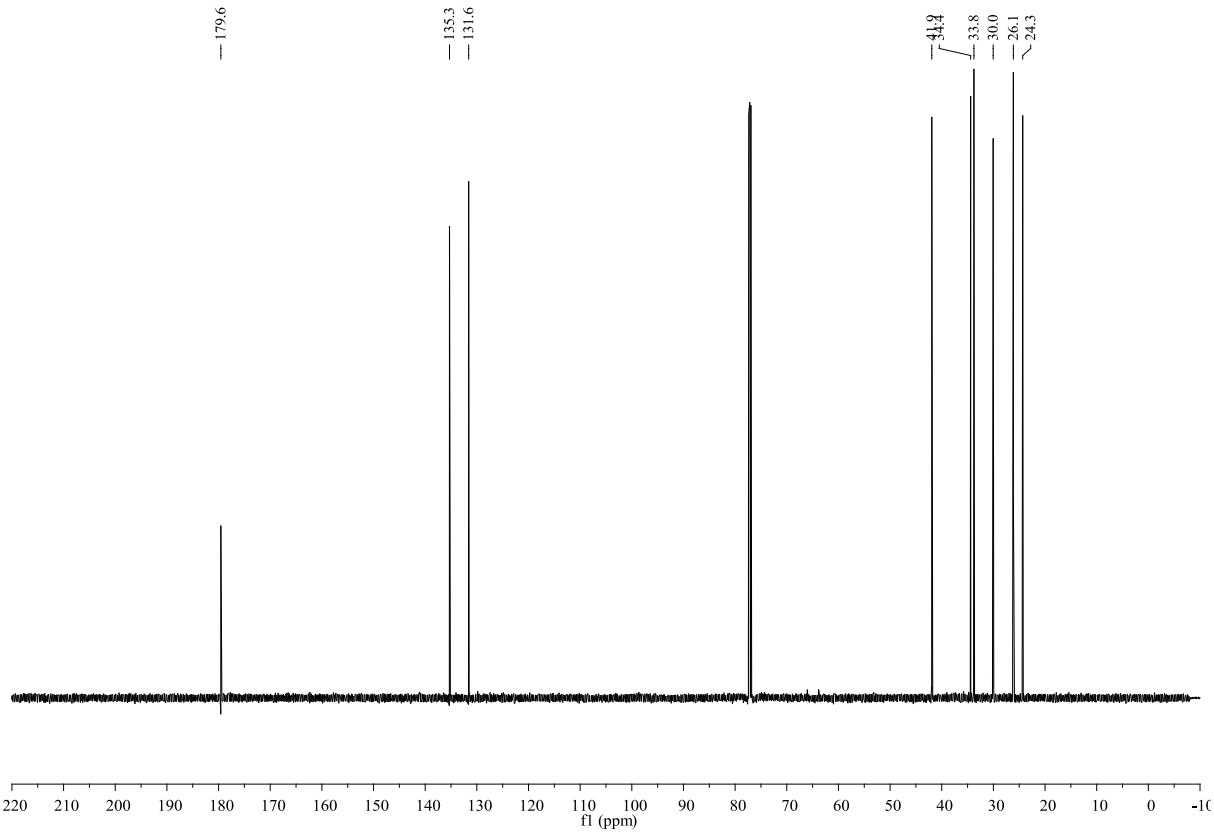


248 (^{1}H NMR, 600 MHz, $CDCl_3$)

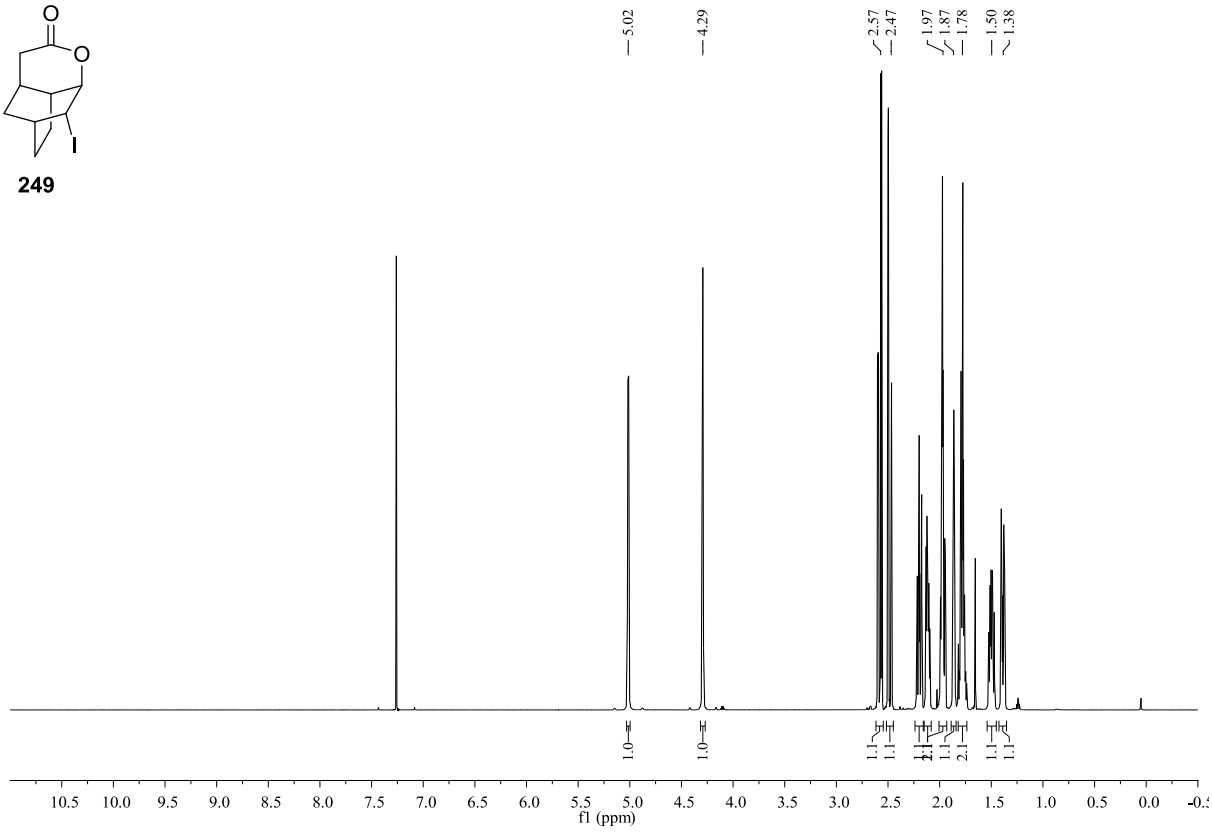


248

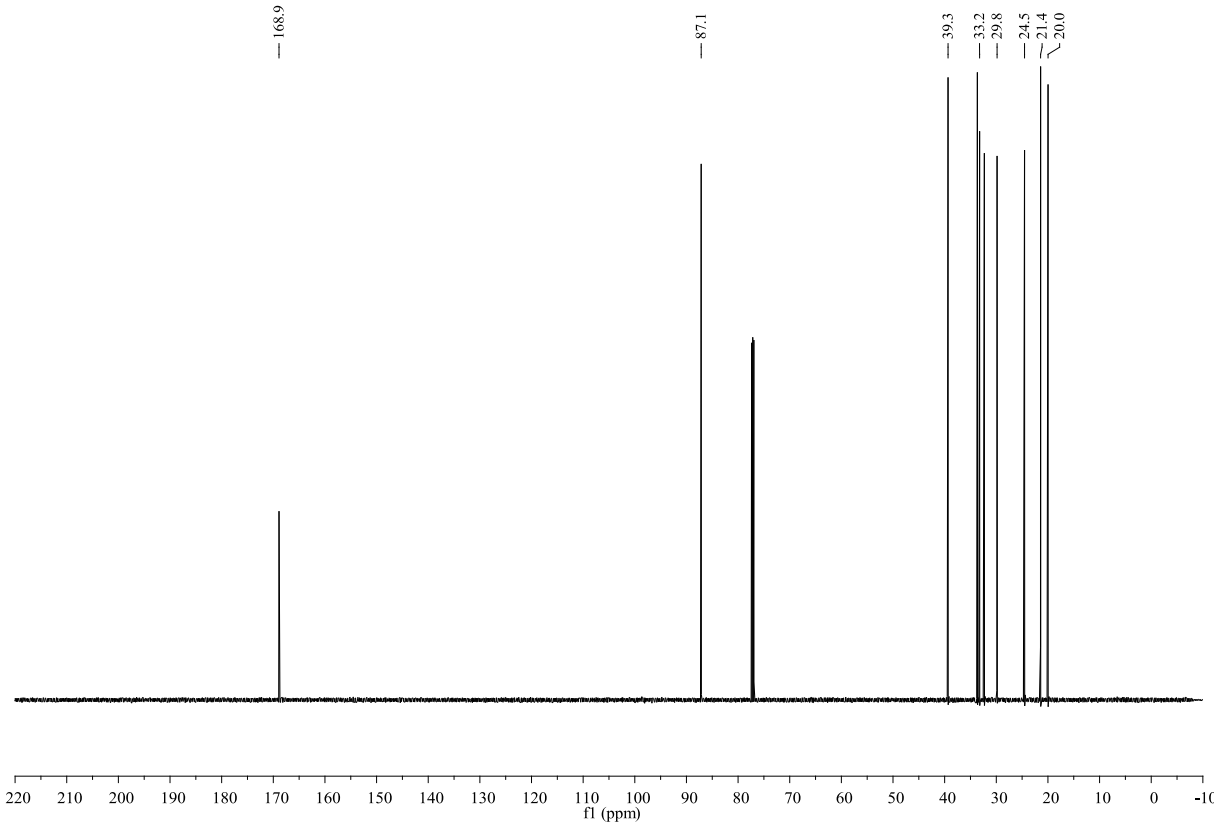
248 (^{13}C NMR, 150 MHz, $CDCl_3$)



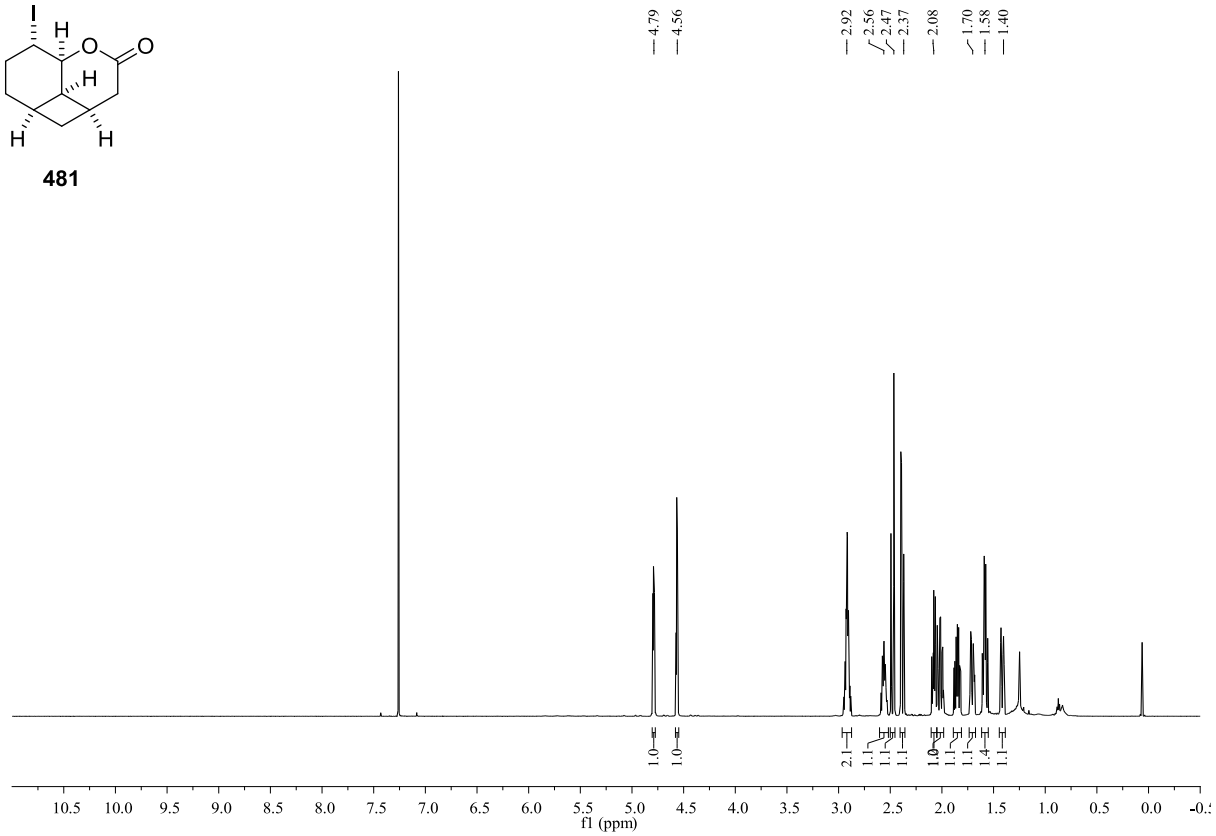
249 (^{1}H NMR, 600 MHz, $CDCl_3$)



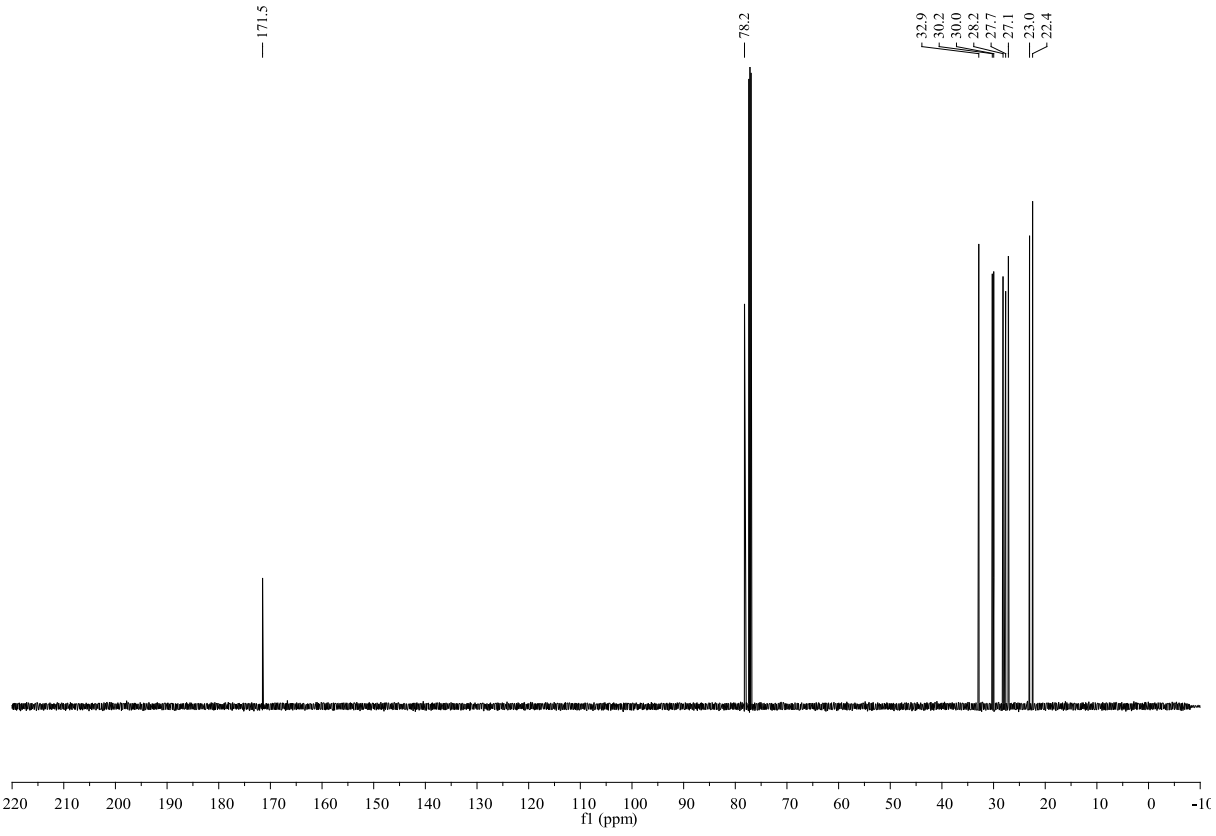
249 (^{13}C NMR, 150 MHz, $CDCl_3$)



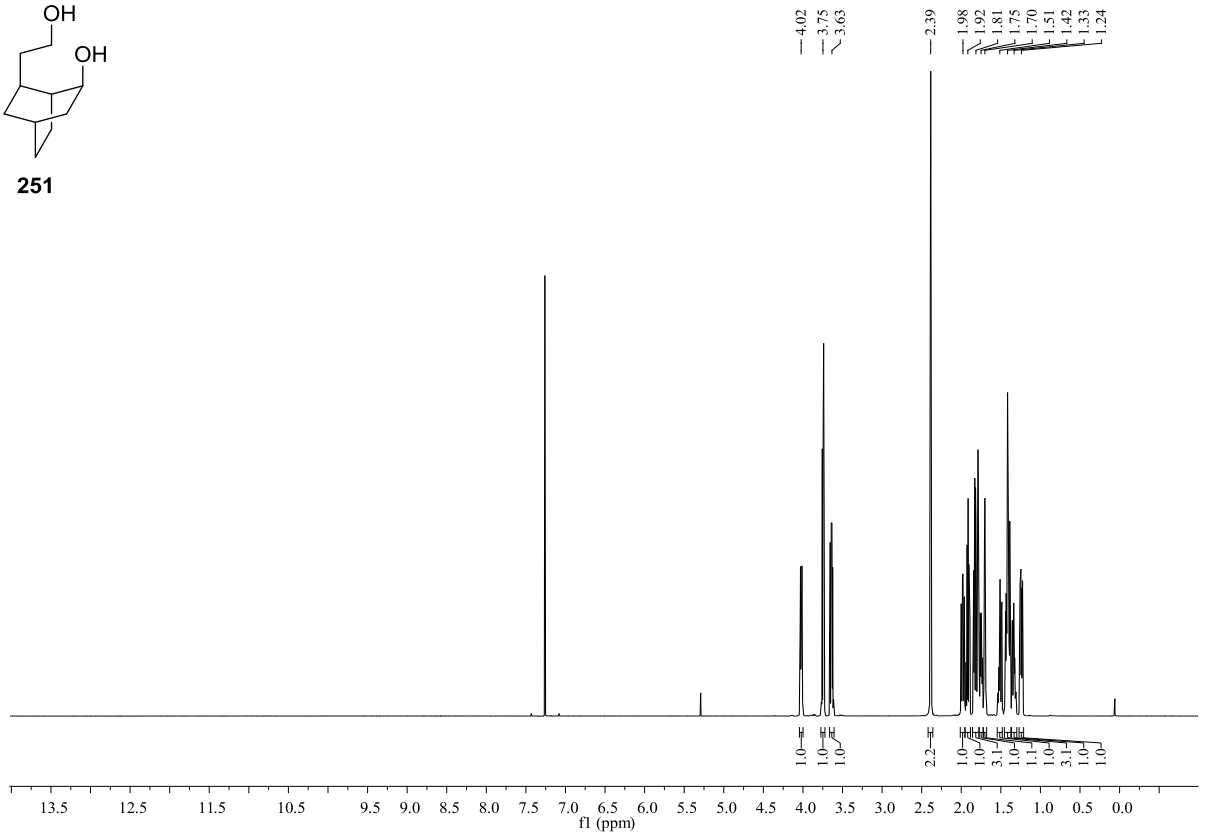
481 (^{1}H NMR, 600 MHz, $CDCl_3$)



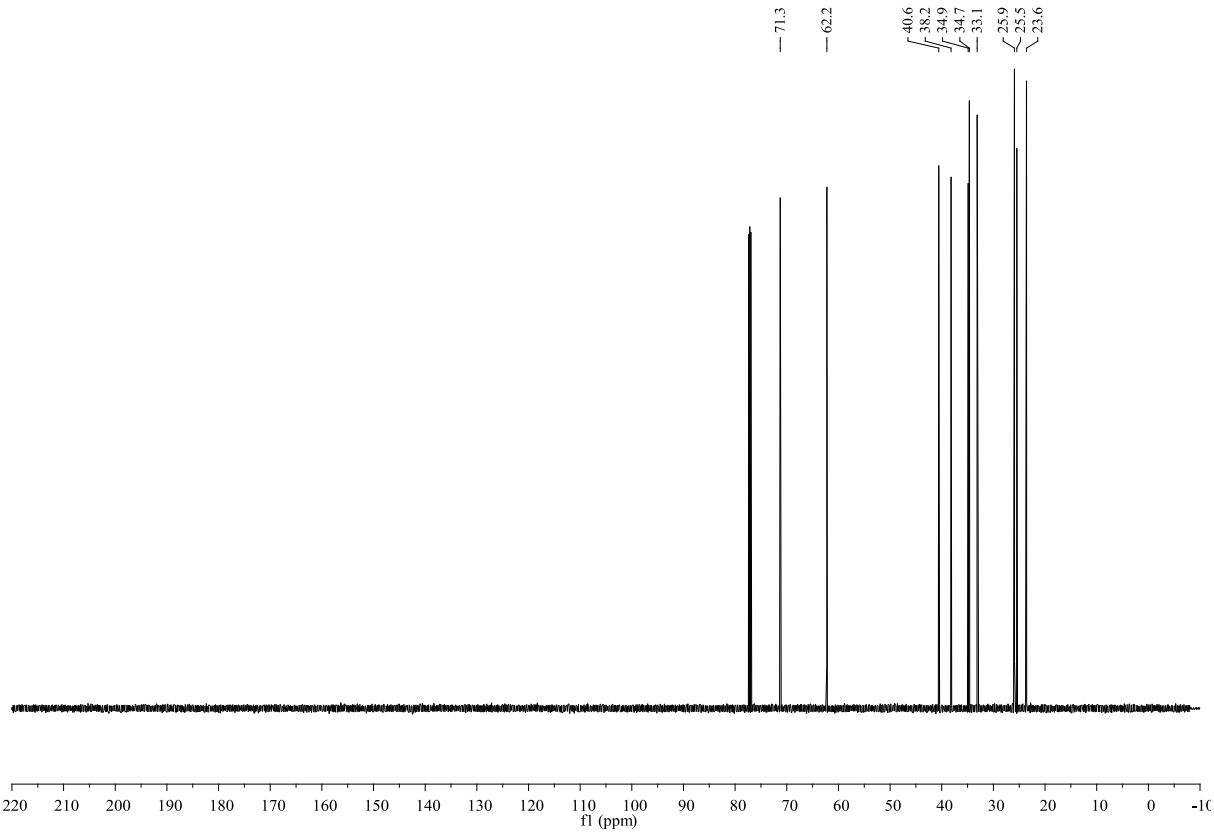
481 (^{13}C NMR, 150 MHz, $CDCl_3$)



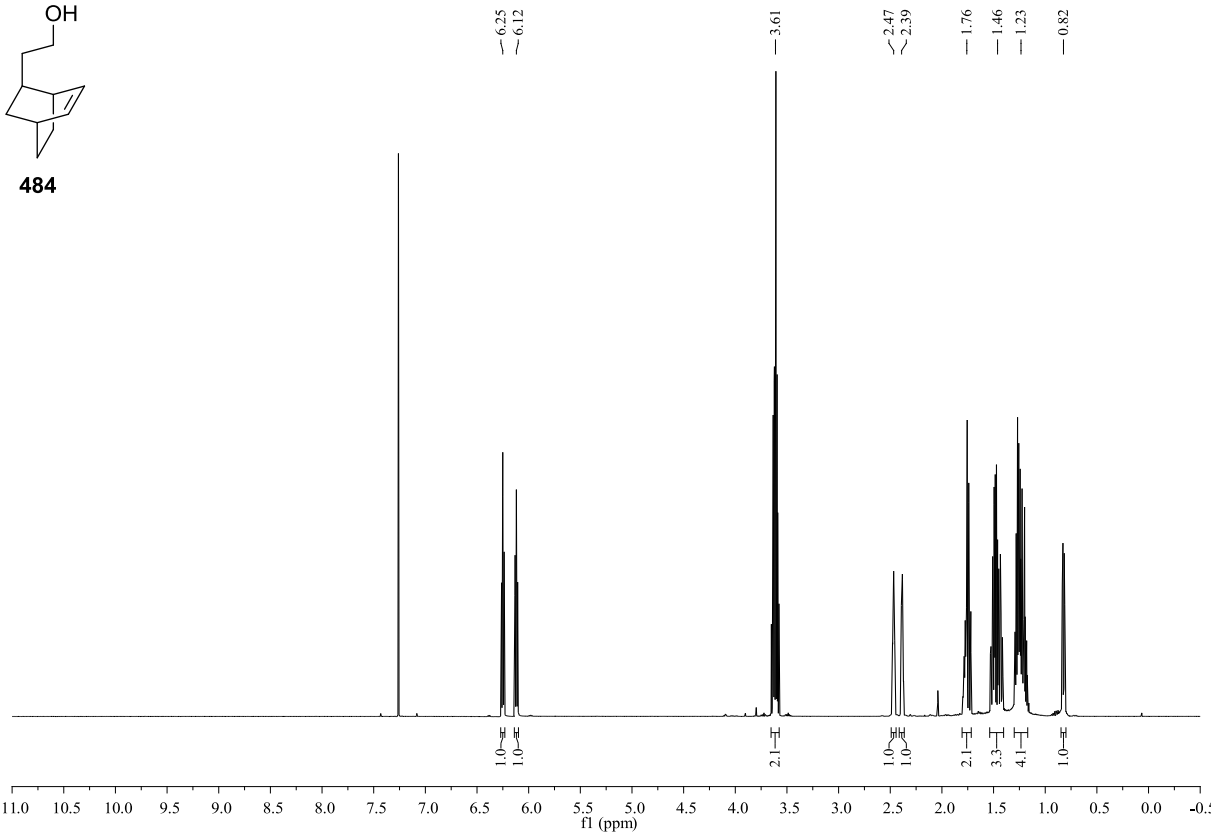
251 (^{1}H NMR, 600 MHz, $CDCl_3$)



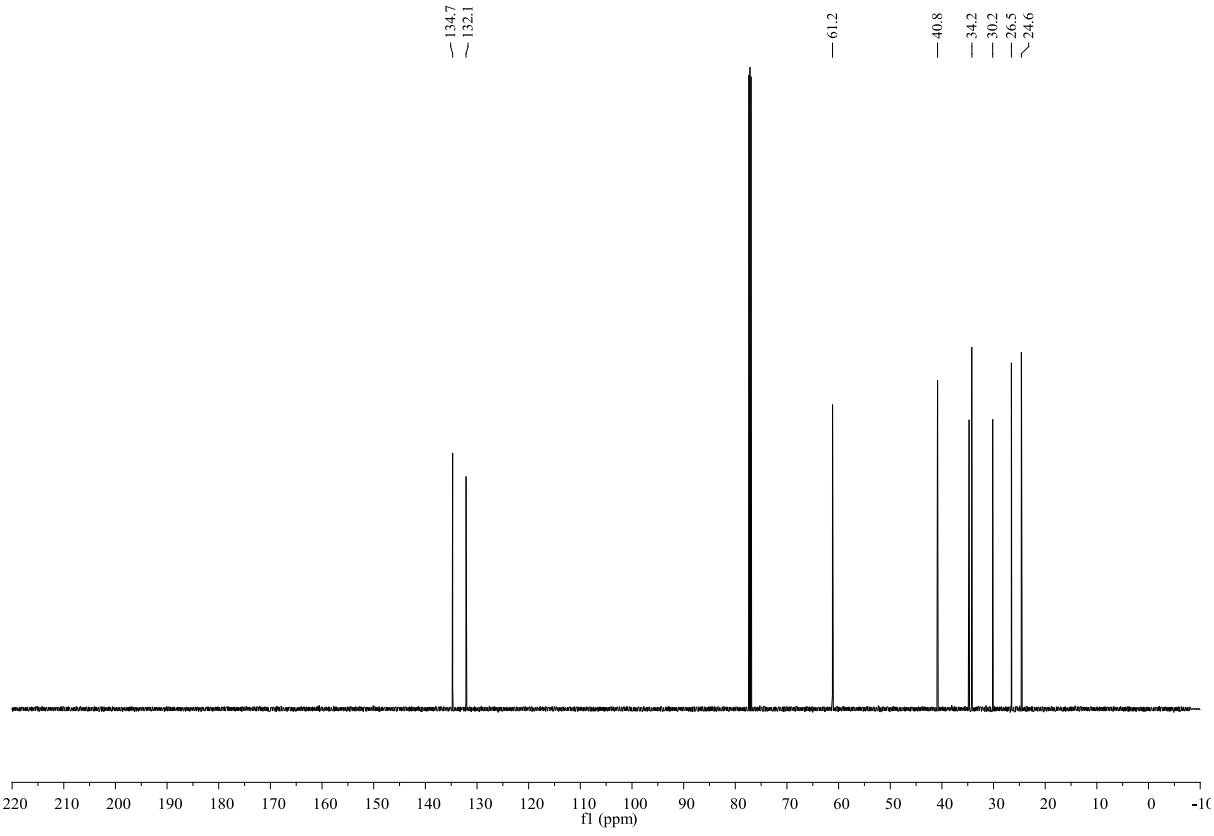
251 (^{13}C NMR, 150 MHz, $CDCl_3$)



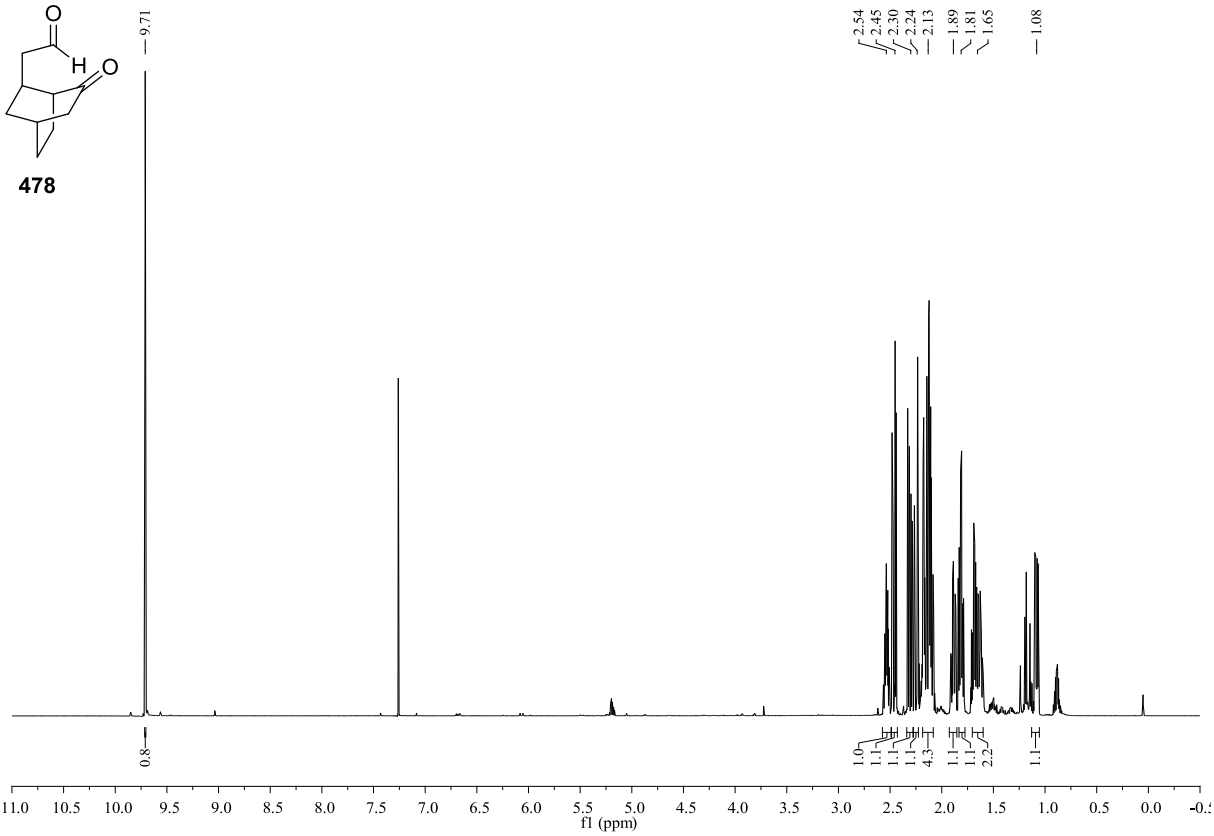
484 (^{1}H NMR, 600 MHz, $CDCl_3$)



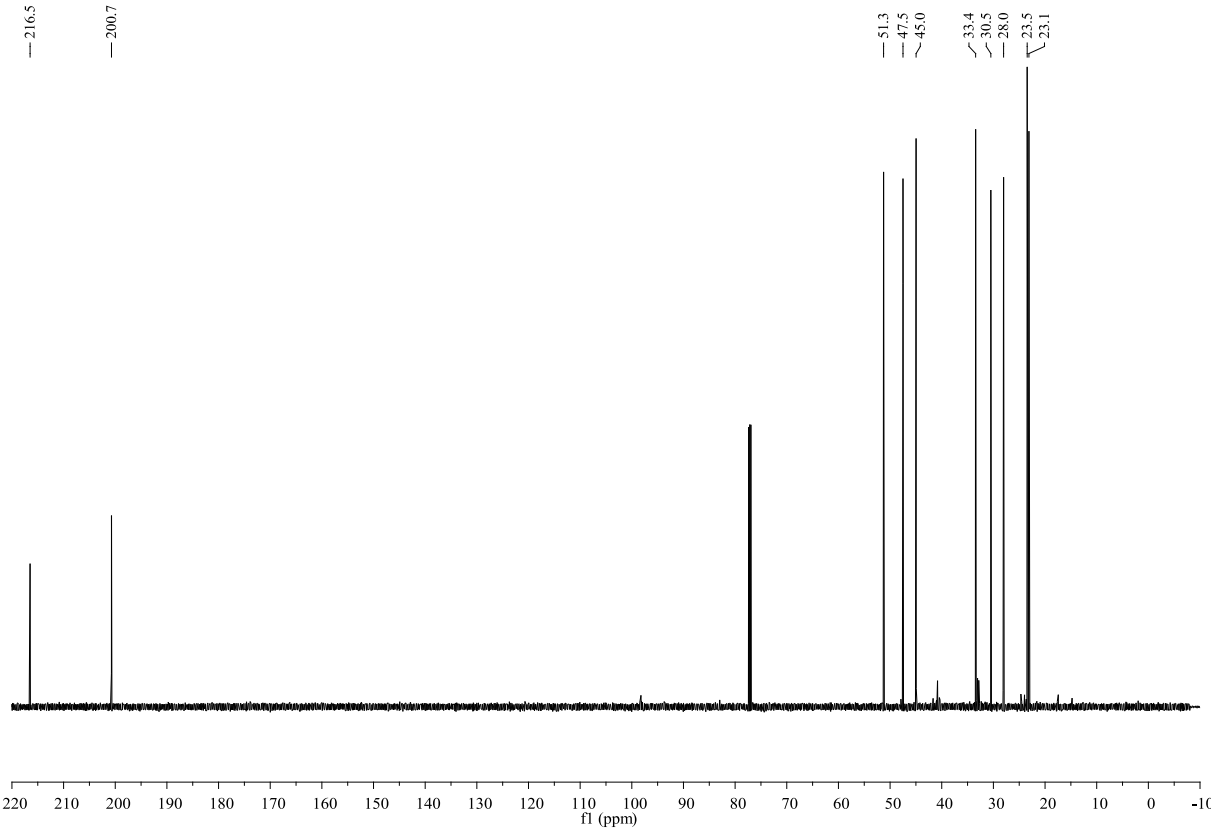
484 (^{13}C NMR, 150 MHz, $CDCl_3$)



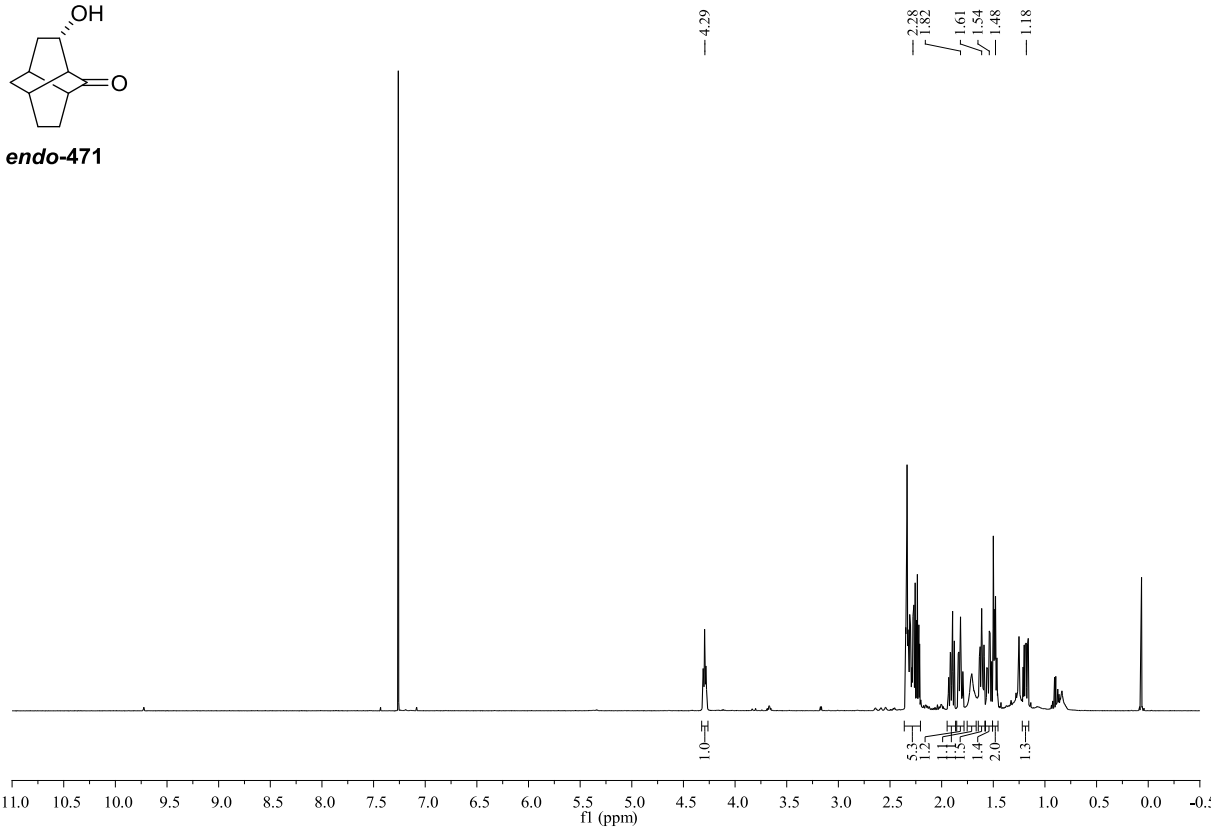
478 (^{1}H NMR, 600 MHz, $CDCl_3$)



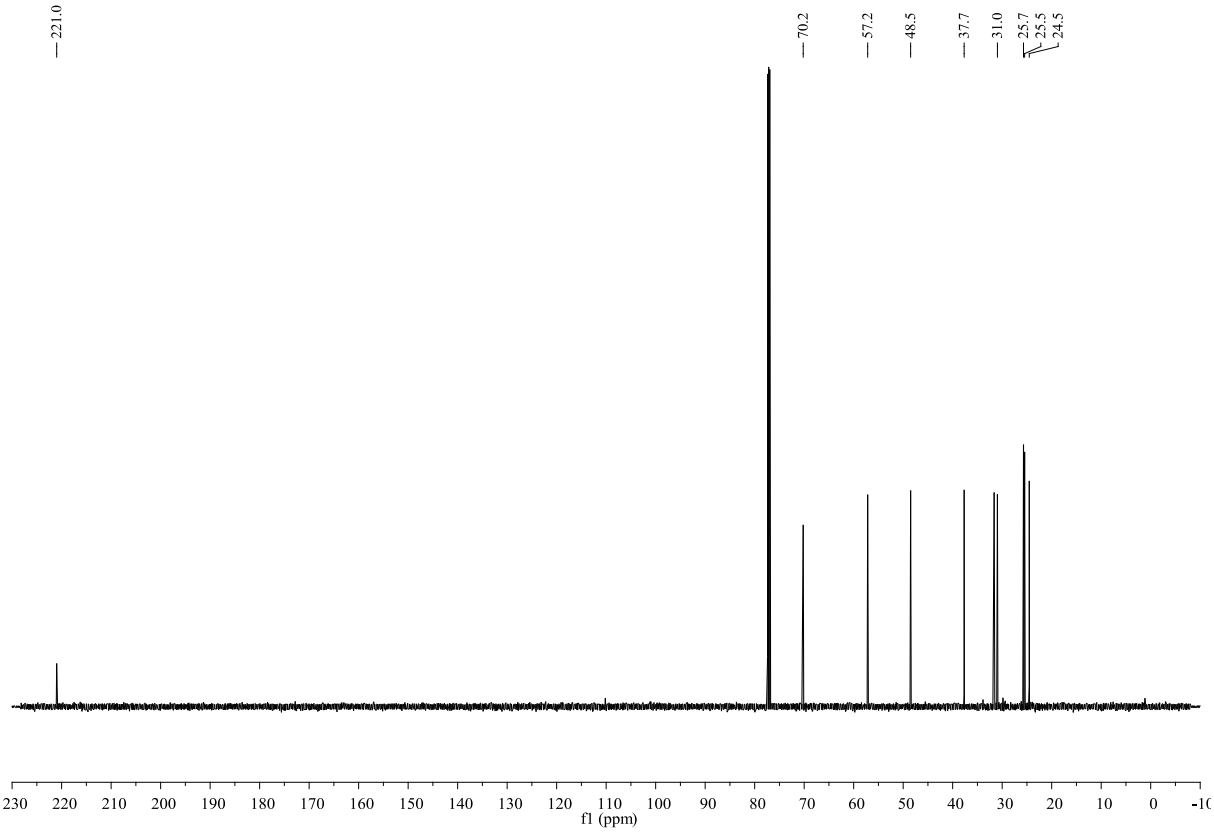
478 (^{13}C NMR, 150 MHz, $CDCl_3$)



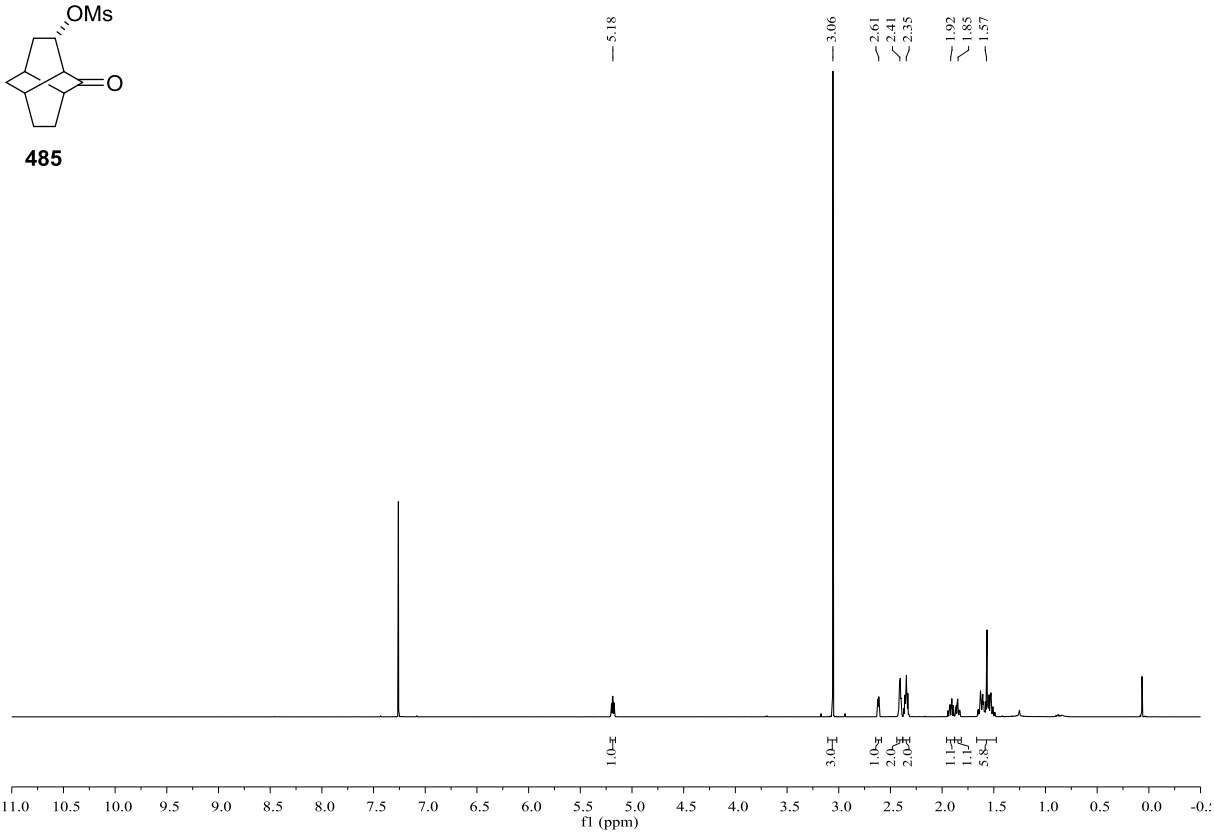
***endo*-471** (^{1}H NMR, 600 MHz, $CDCl_3$)



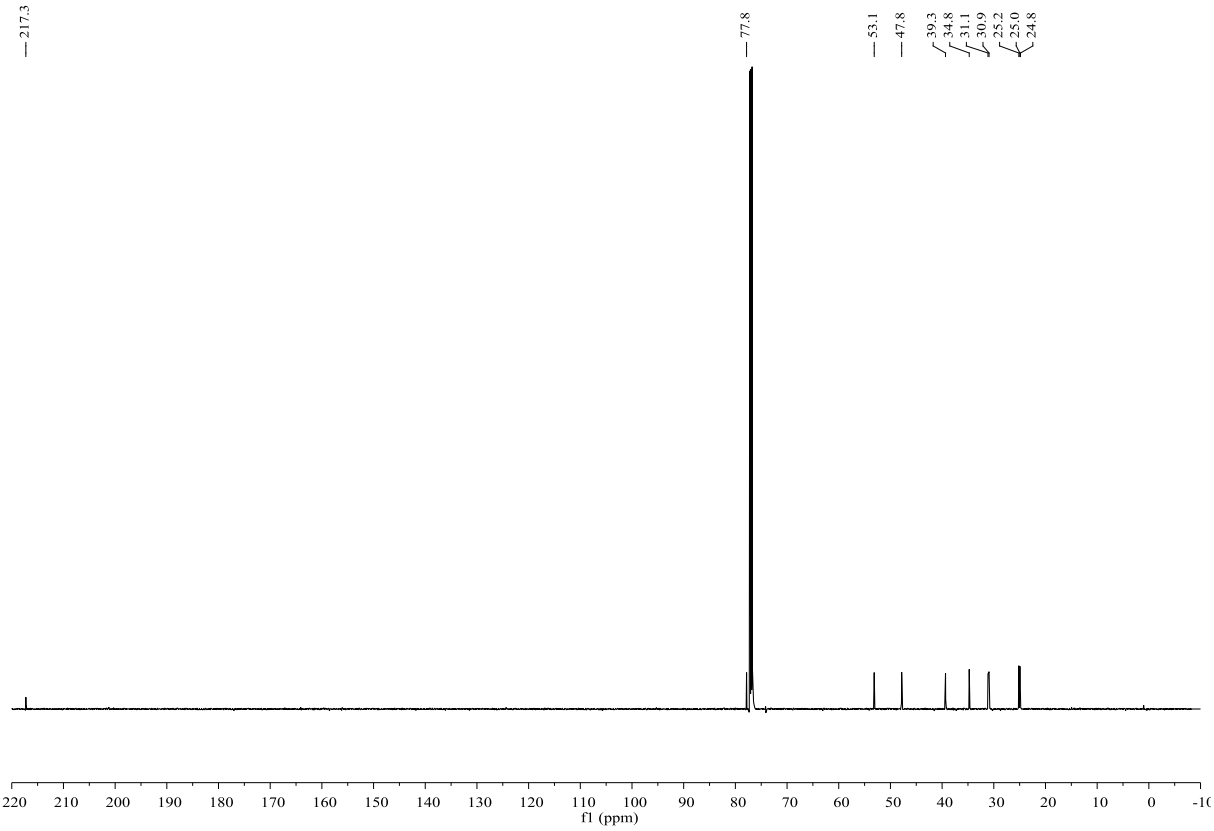
***endo*-471** (^{13}C NMR, 150 MHz, $CDCl_3$)



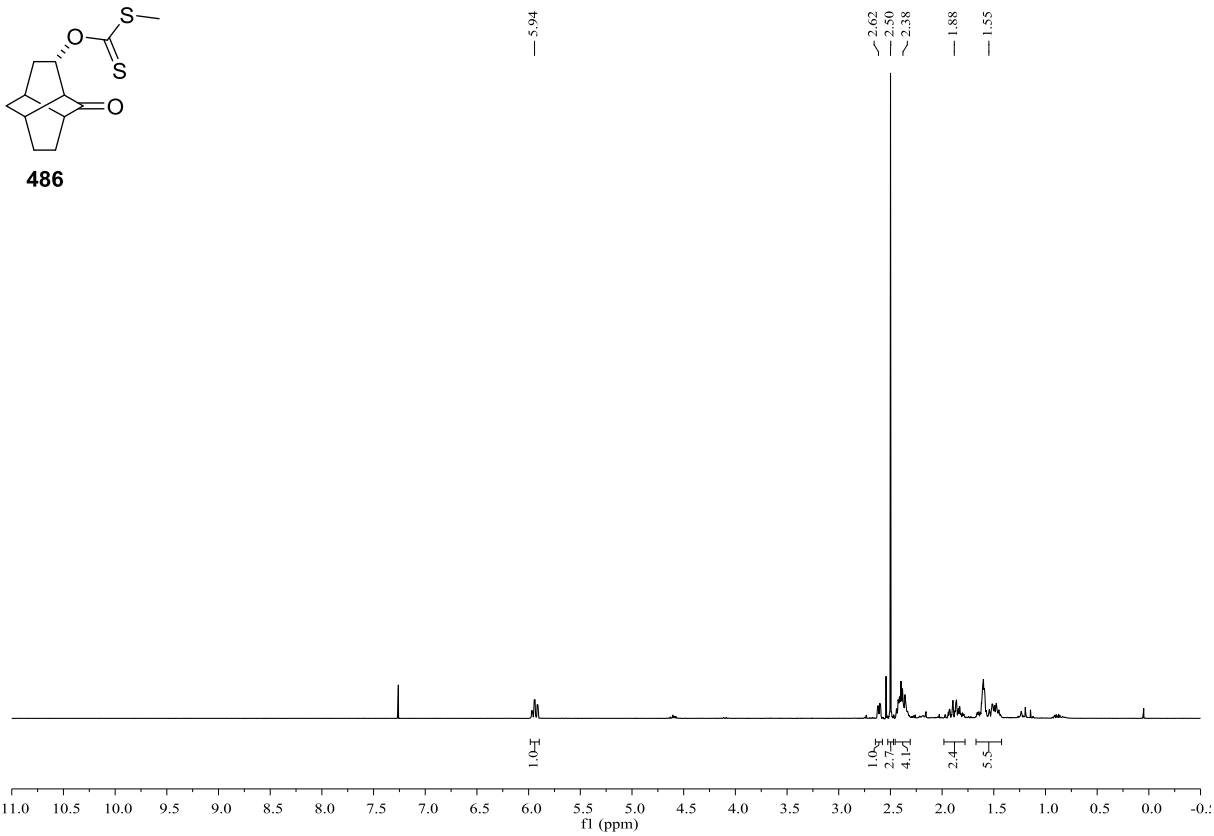
485 (^{1}H NMR, 600 MHz, $CDCl_3$)



485 (^{13}C NMR, 150 MHz, $CDCl_3$)

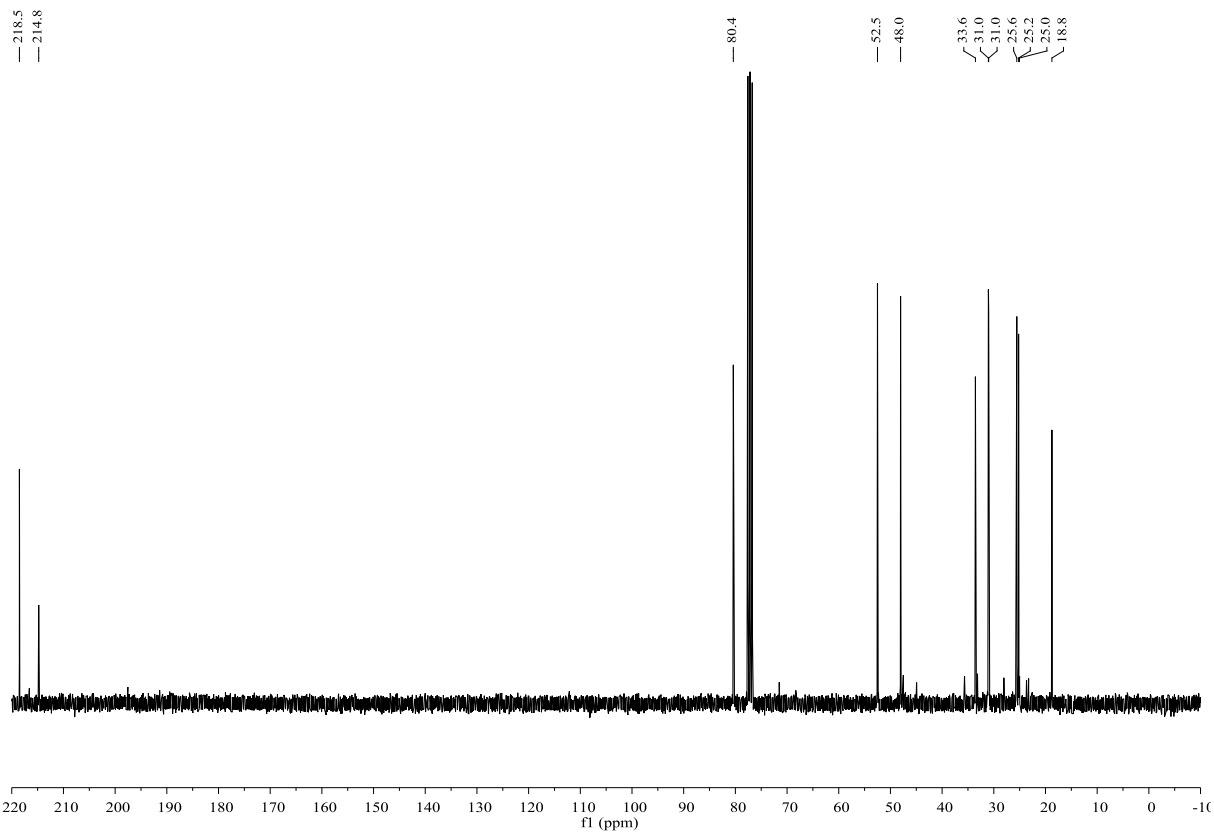


486 (^{1}H NMR, 300 MHz, $CDCl_3$)

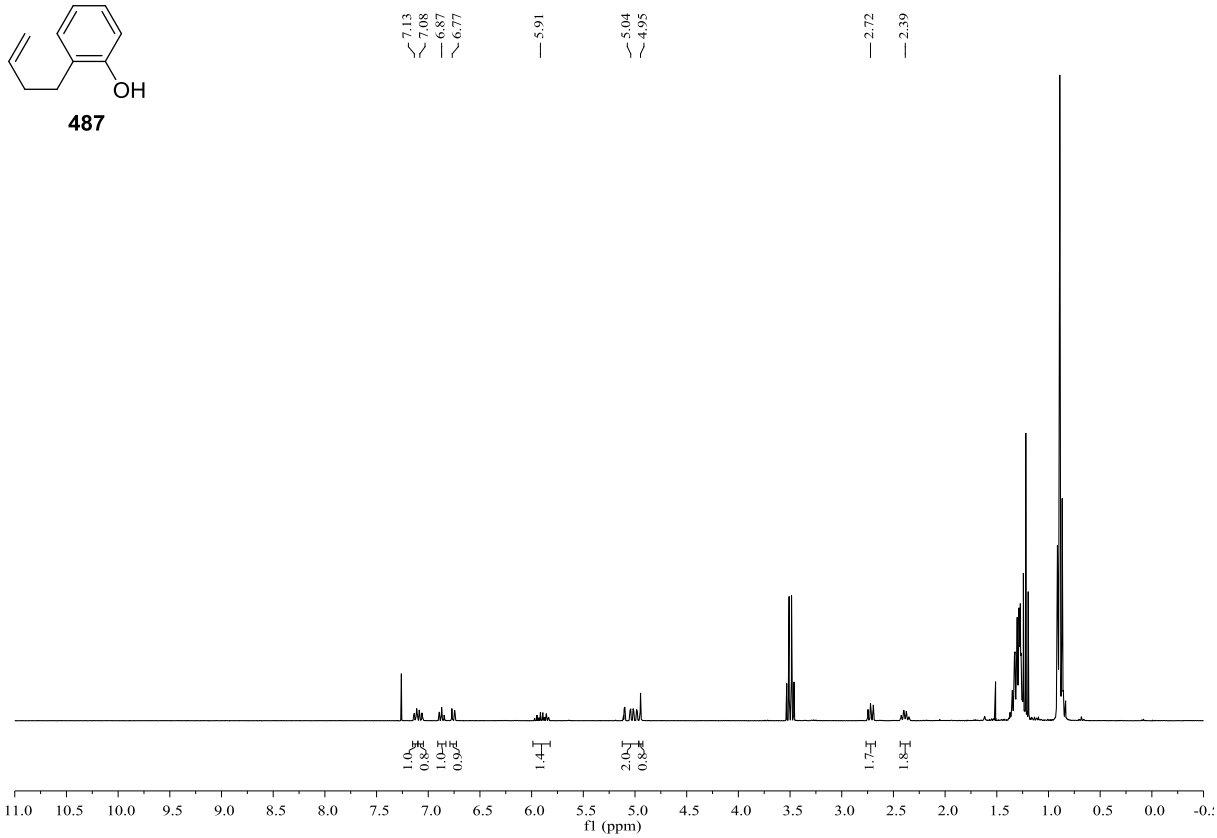


486

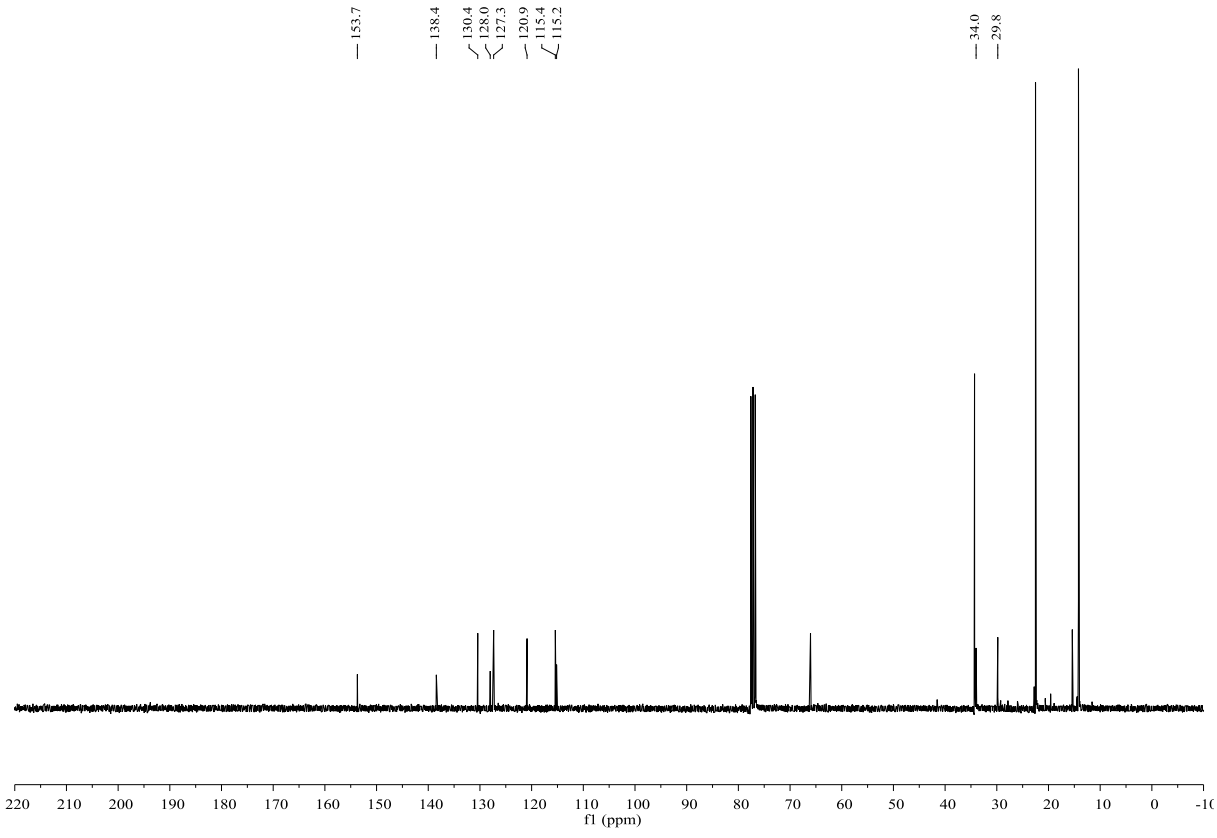
486 (^{13}C NMR, 75 MHz, $CDCl_3$)



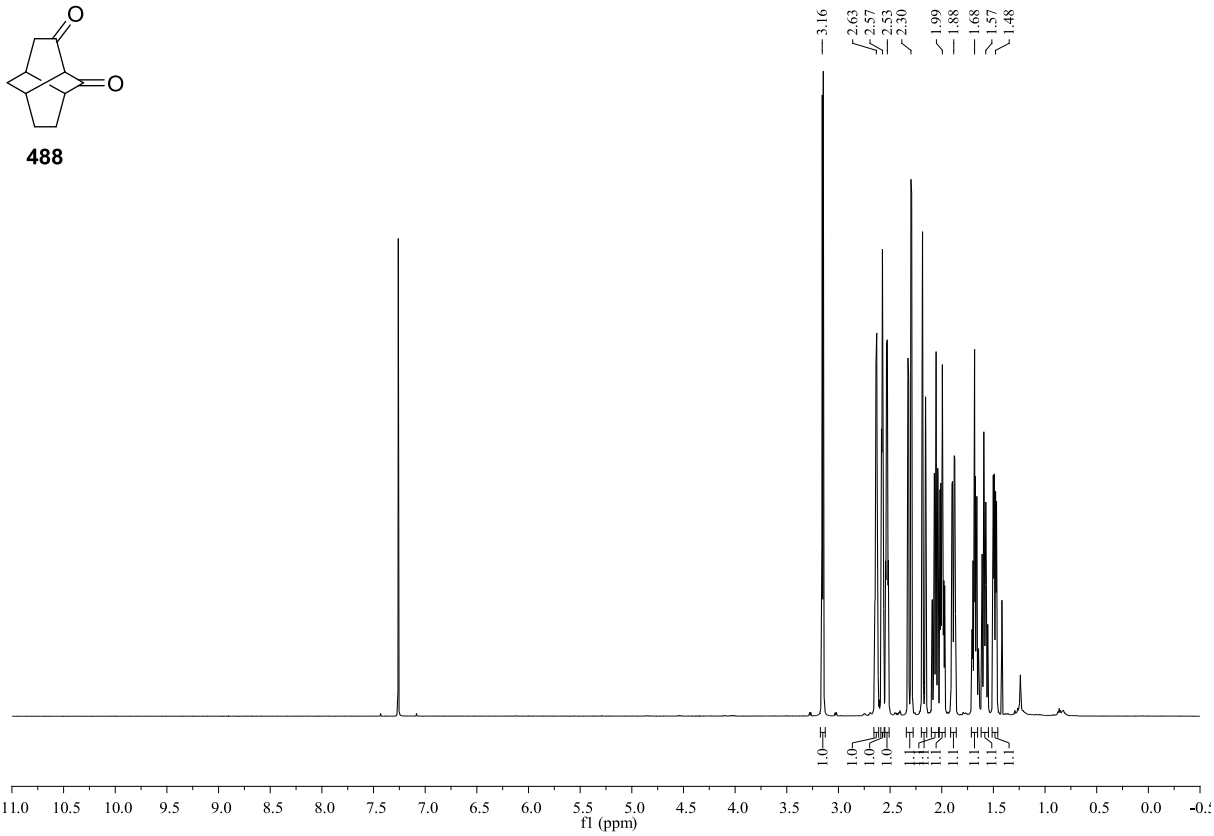
487 (^{1}H NMR, 300 MHz, $CDCl_3$)



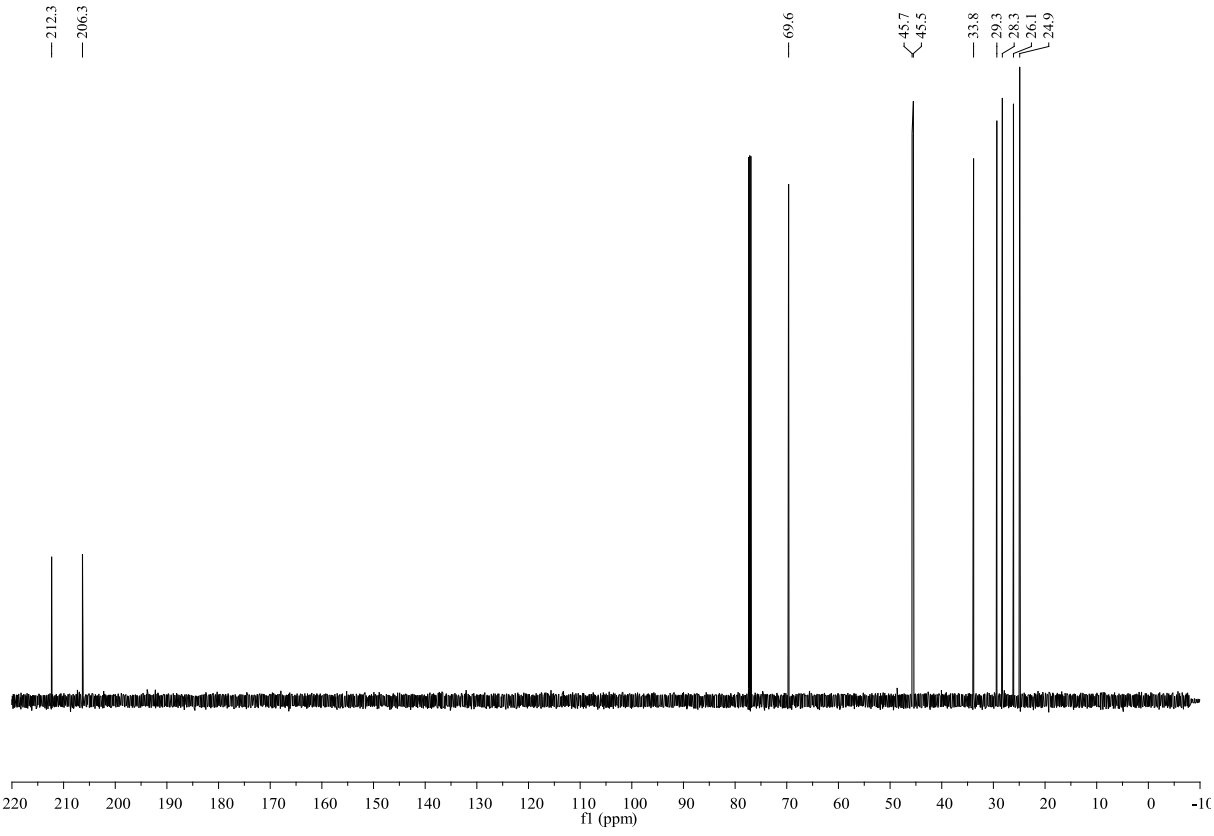
487 (^{13}C NMR, 75 MHz, $CDCl_3$)



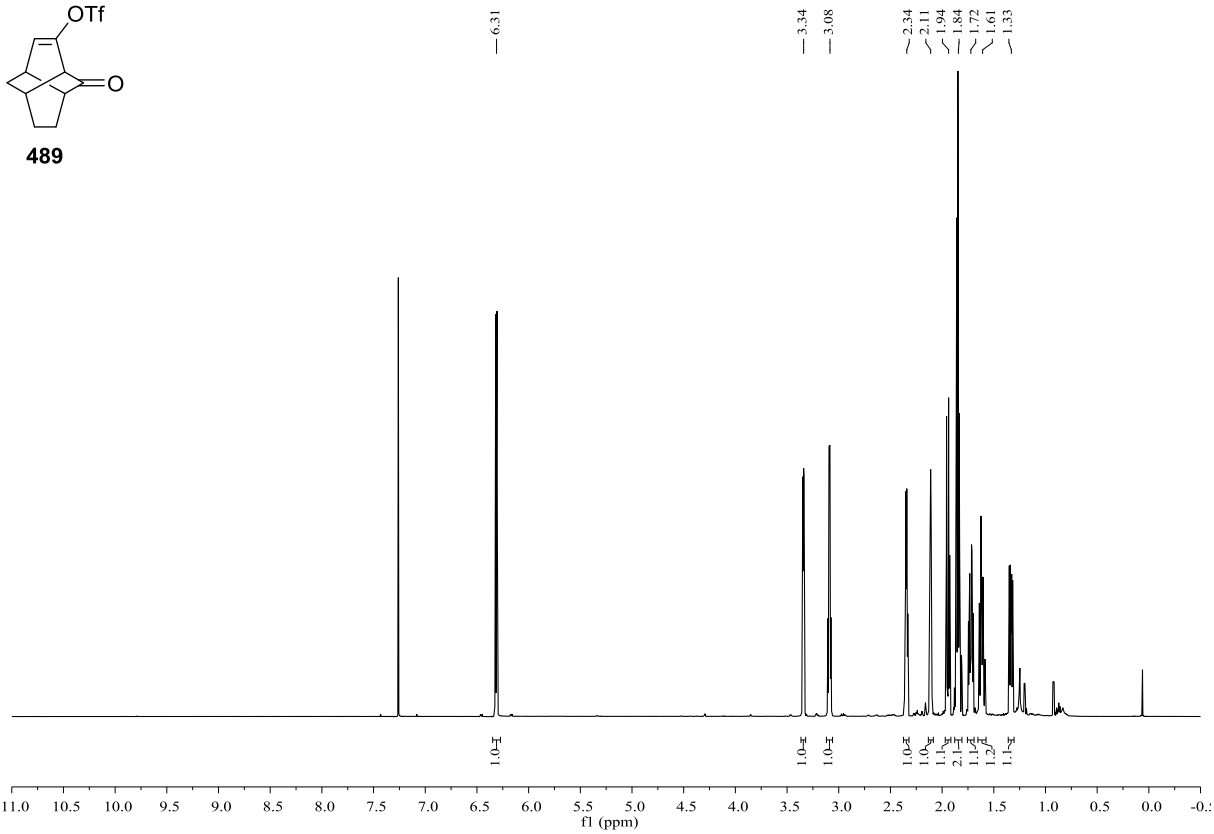
488 (^{1}H NMR, 600 MHz, $CDCl_3$)



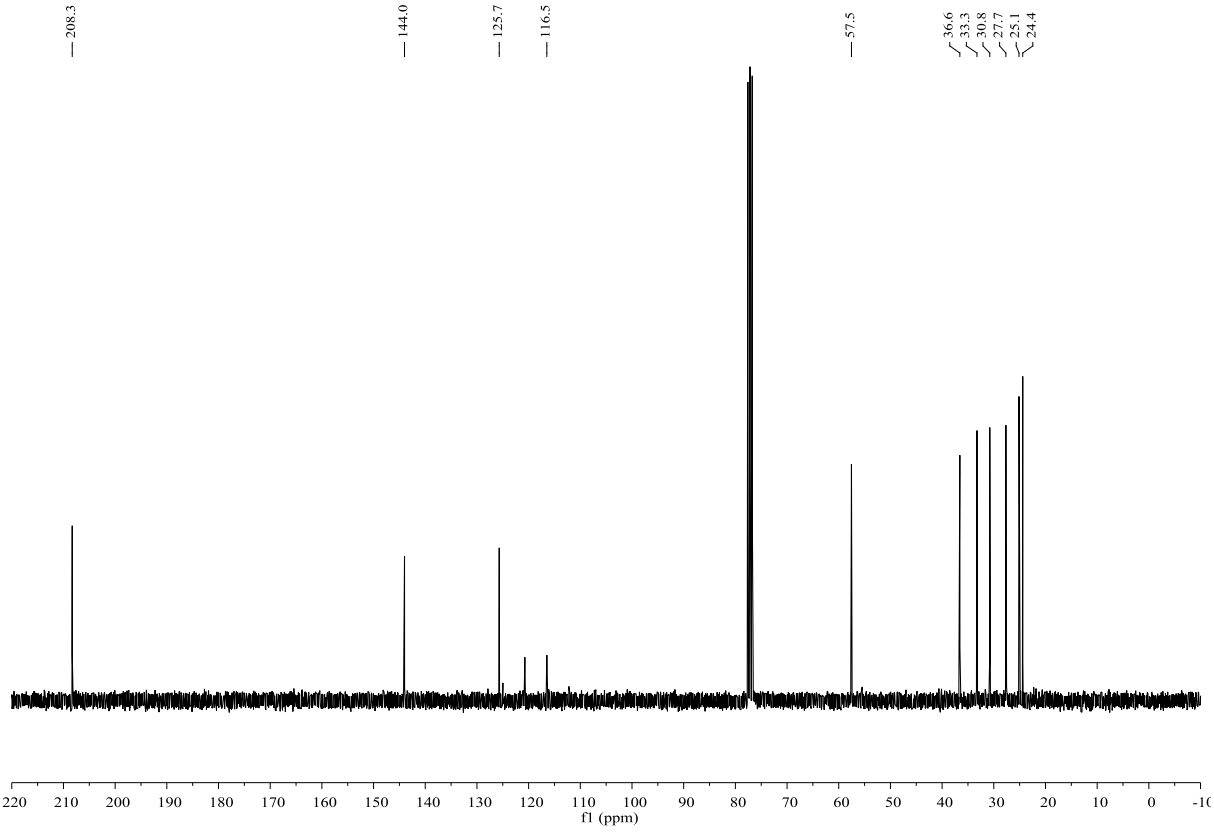
488 (^{13}C NMR, 150 MHz, $CDCl_3$)



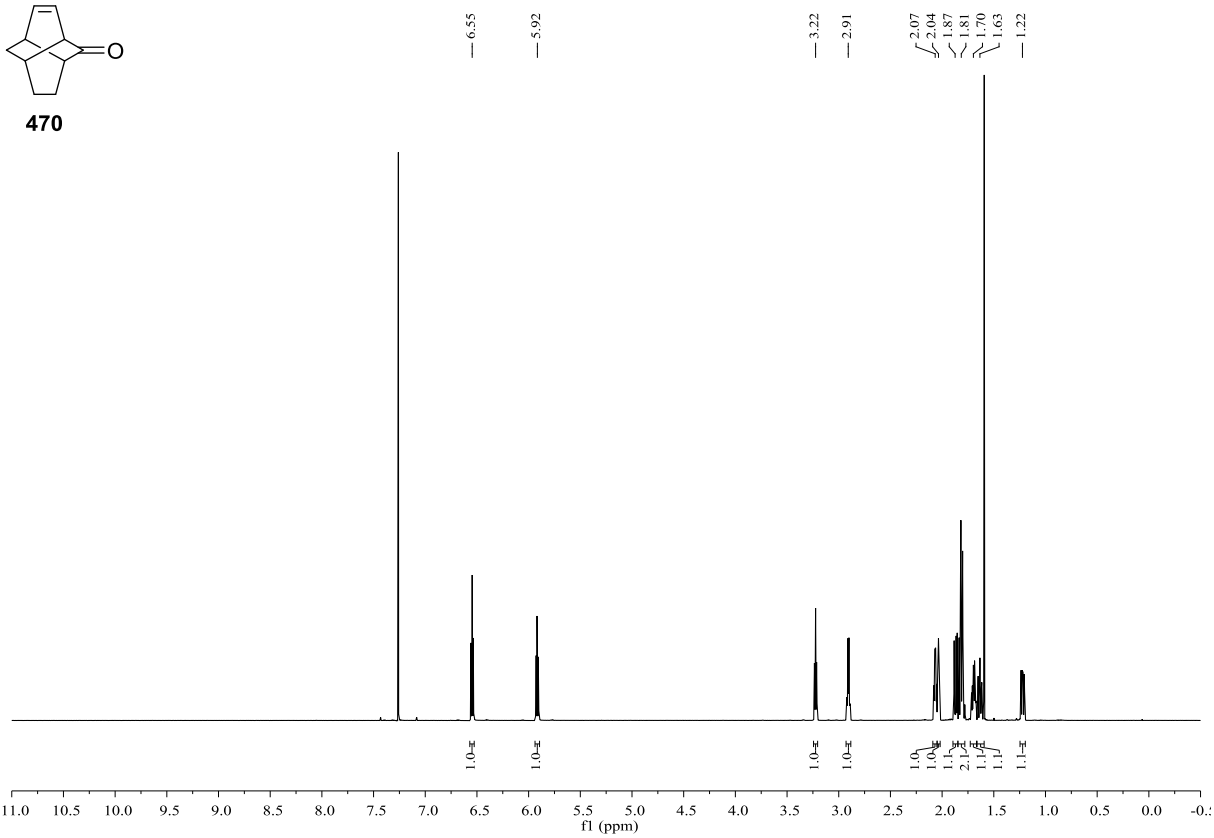
489 (^{1}H NMR, 600 MHz, $CDCl_3$)



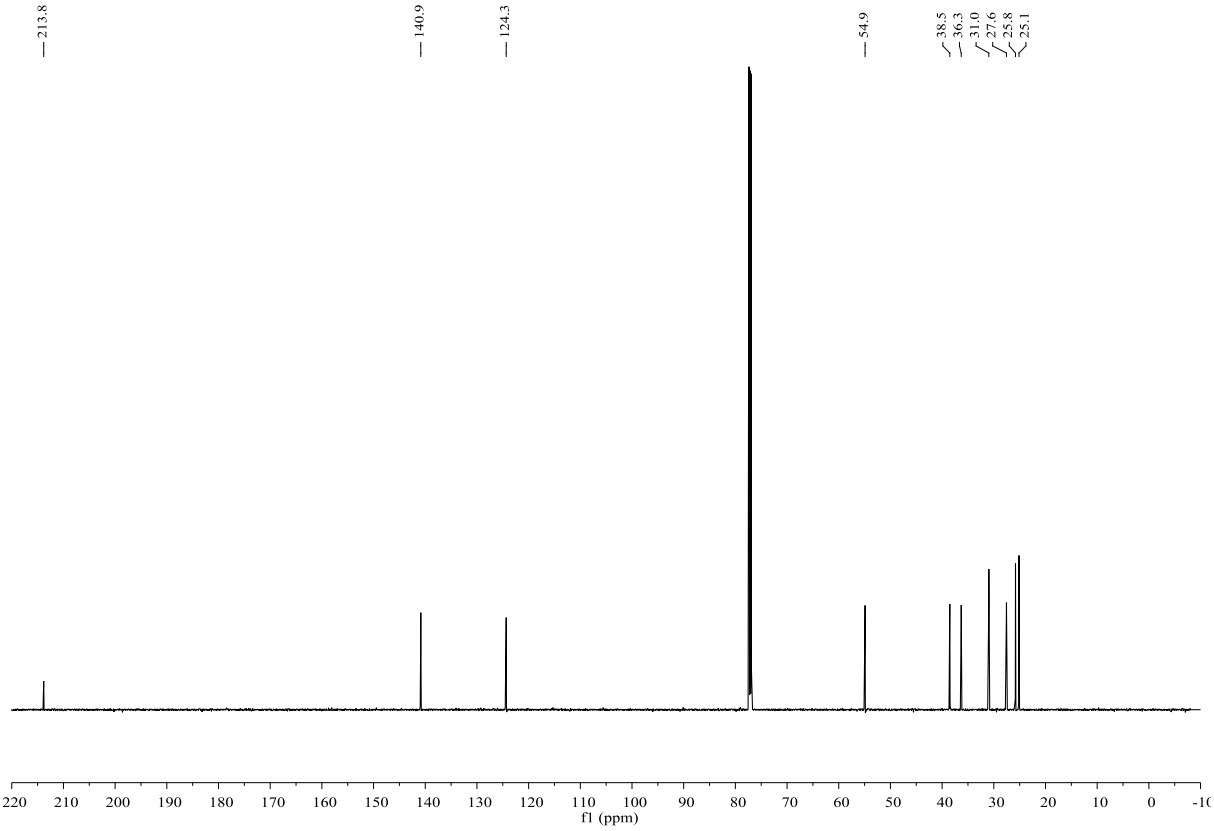
489 (^{13}C NMR, 75 MHz, $CDCl_3$)



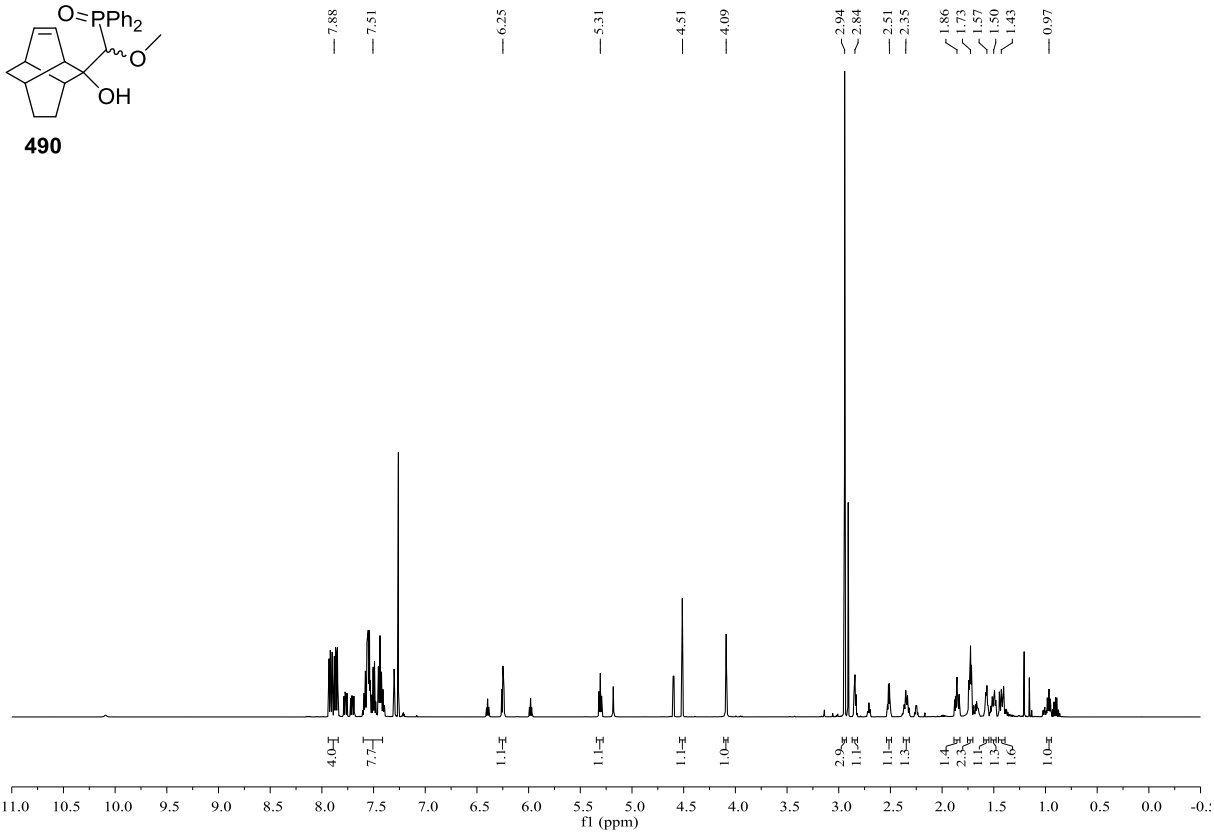
470 (^{1}H NMR, 600 MHz, $CDCl_3$)



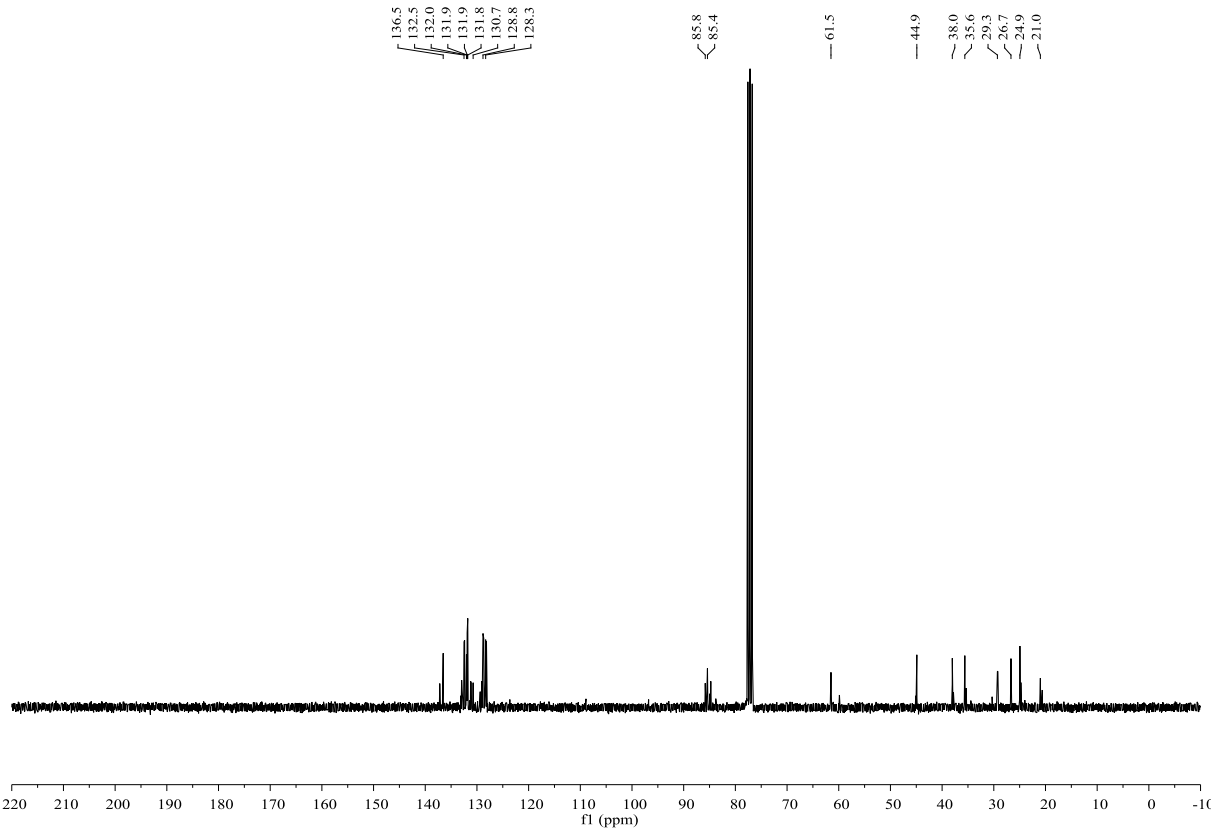
470 (^{13}C NMR, 150 MHz, $CDCl_3$)



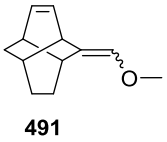
490 (^{1}H NMR, 600 MHz, $CDCl_3$)



490 (^{13}C NMR, 75 MHz, $CDCl_3$)

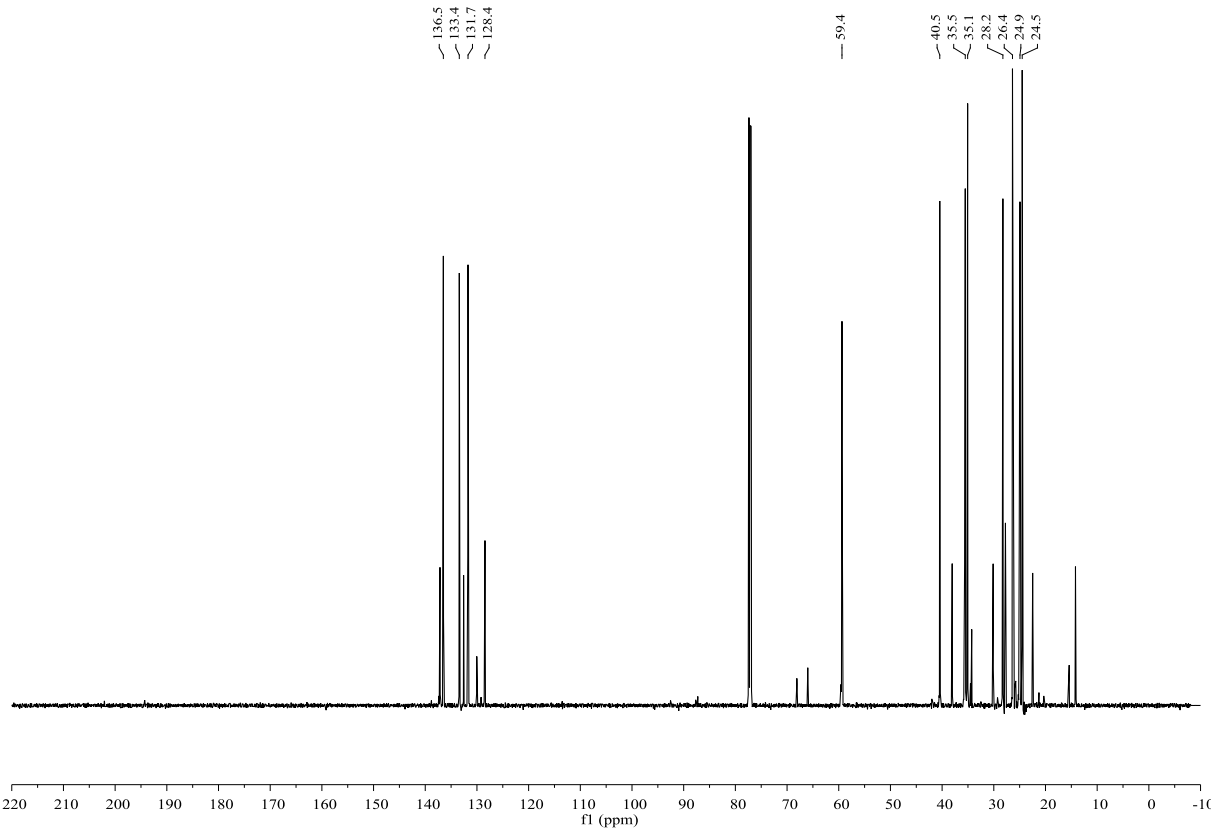


491 (^{1}H NMR, 600 MHz, $CDCl_3$)

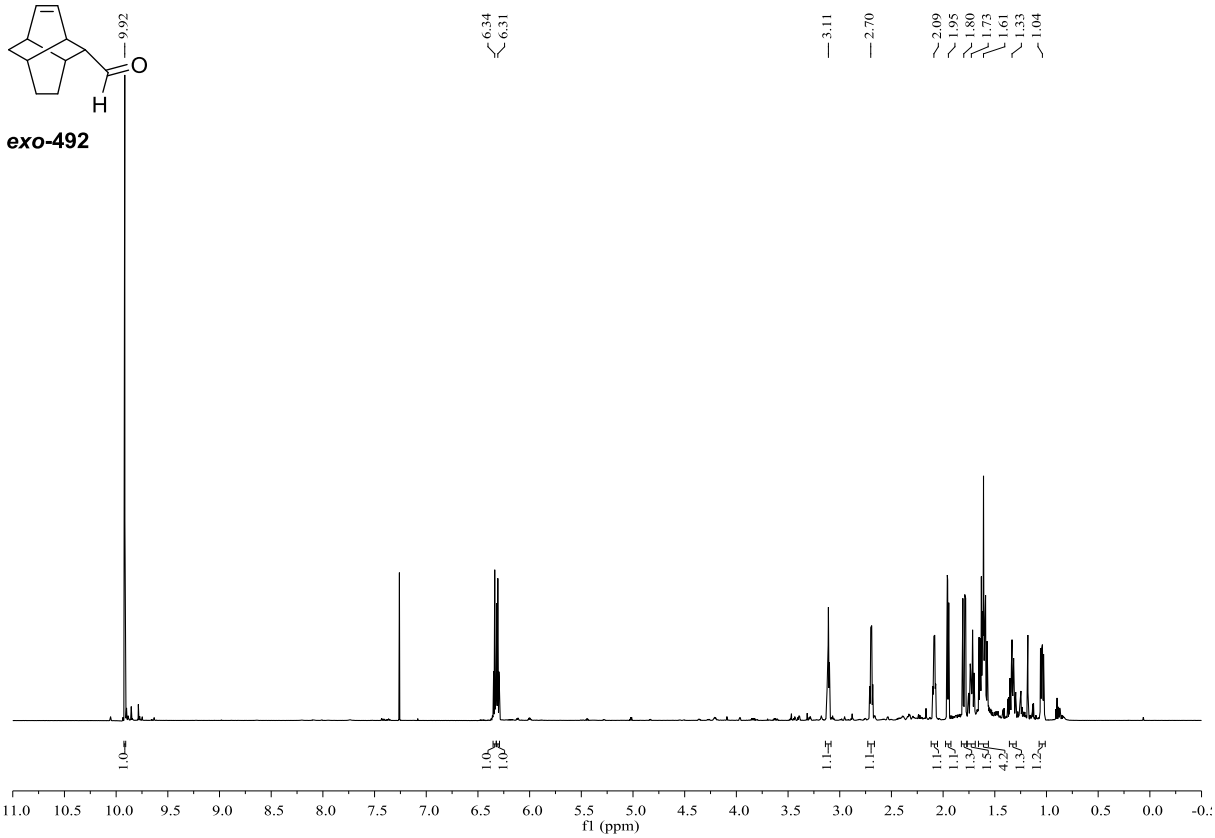


491

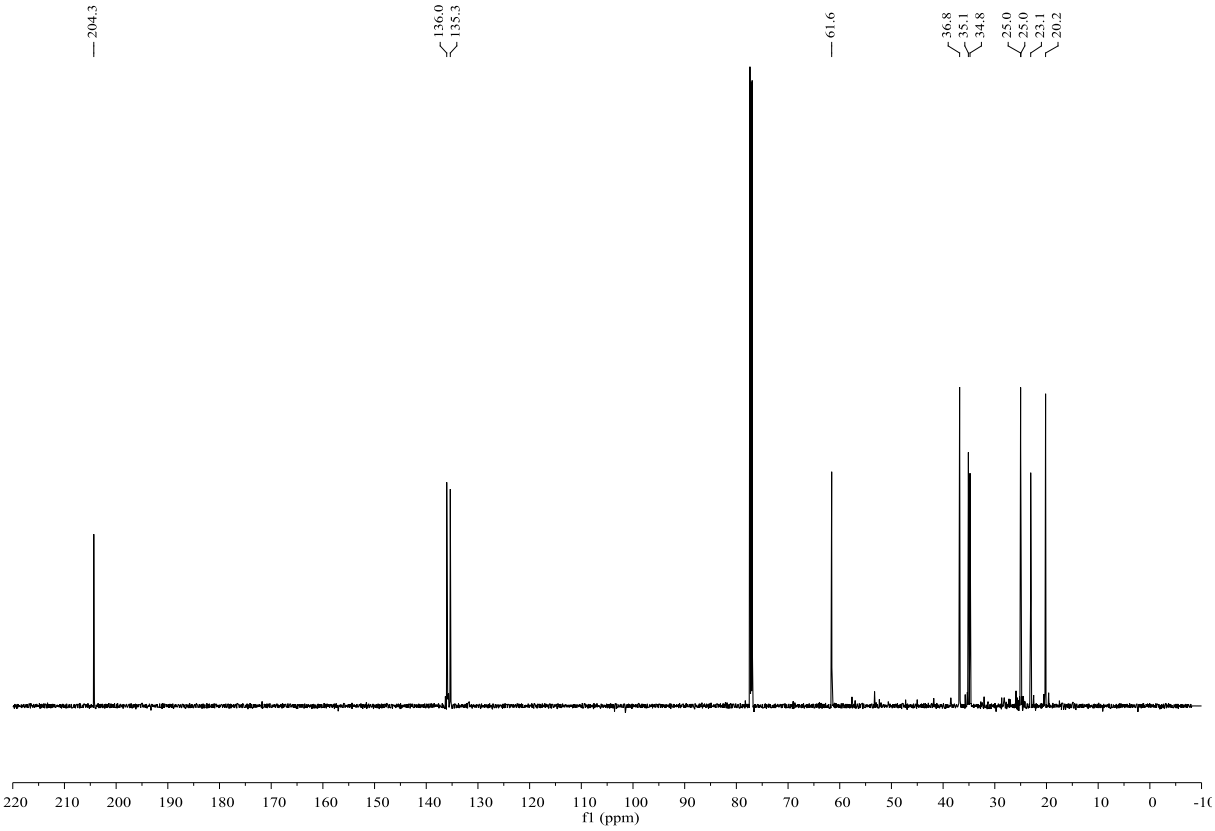
491 (^{13}C NMR, 150 MHz, $CDCl_3$)



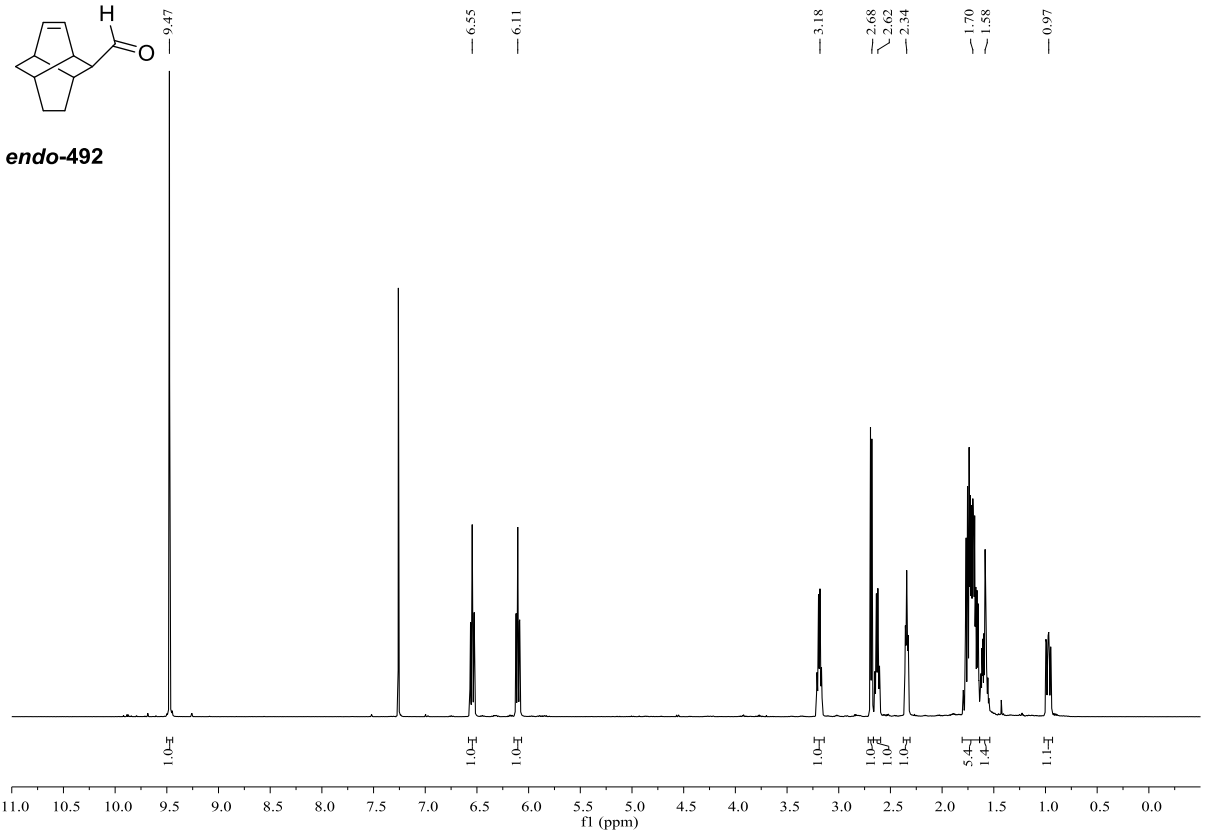
***exo*-492** (^{1}H NMR, 600 MHz, $CDCl_3$)



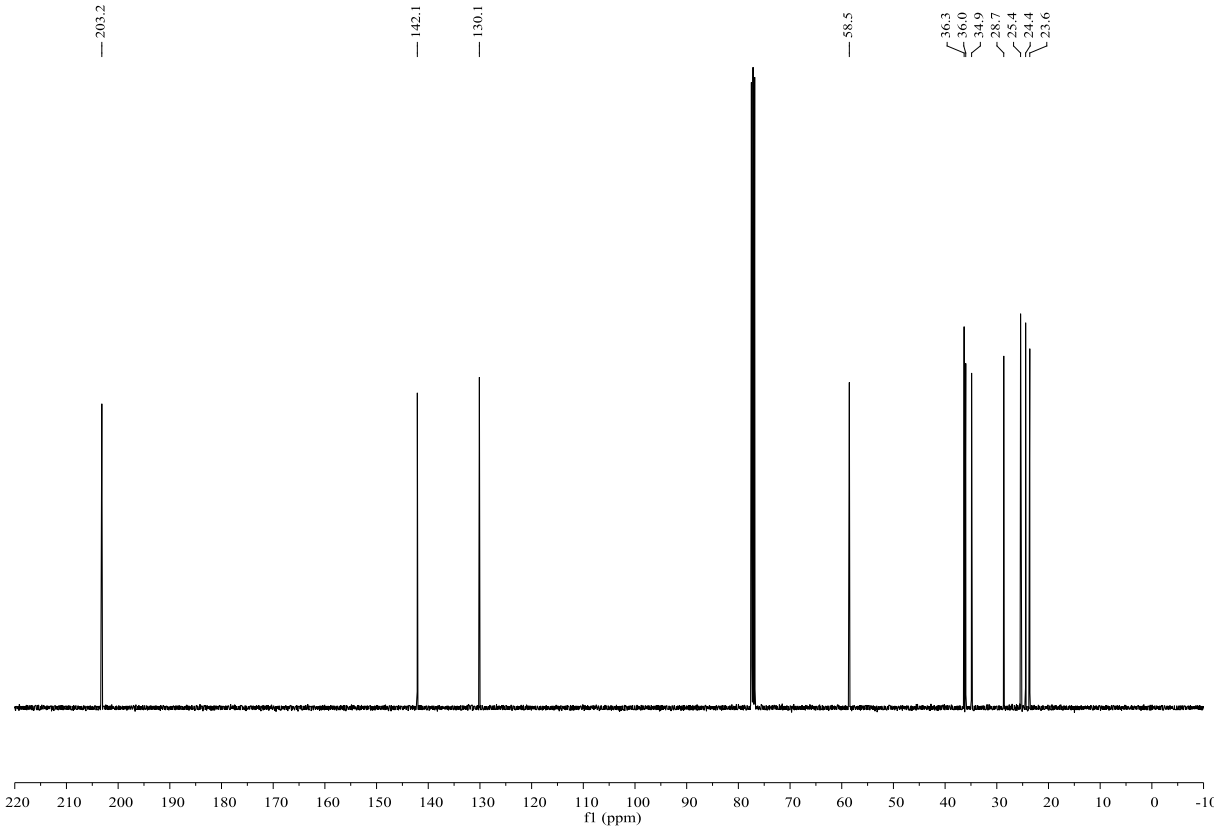
***exo*-492** (^{13}C NMR, 150 MHz, $CDCl_3$)



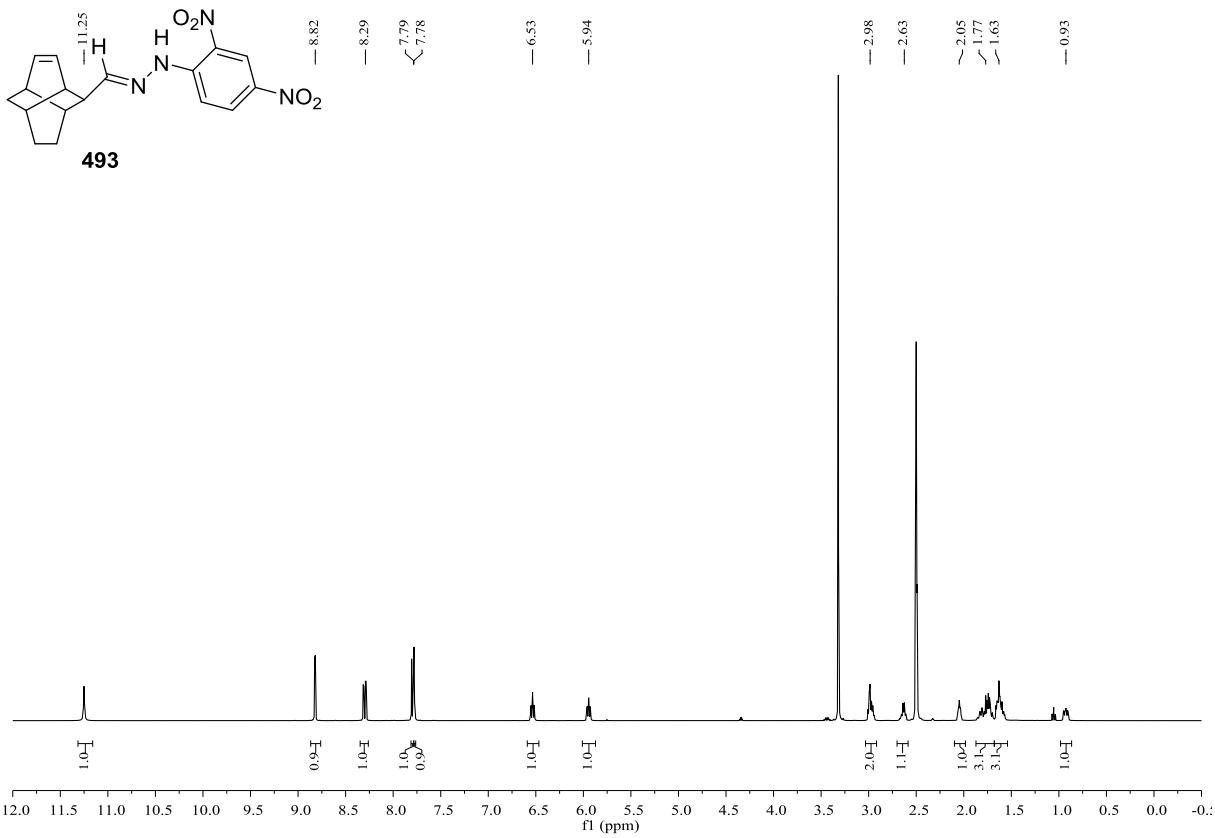
***endo*-492** (^{1}H NMR, 400 MHz, $CDCl_3$)



***endo*-492** (^{13}C NMR, 100 MHz, $CDCl_3$)

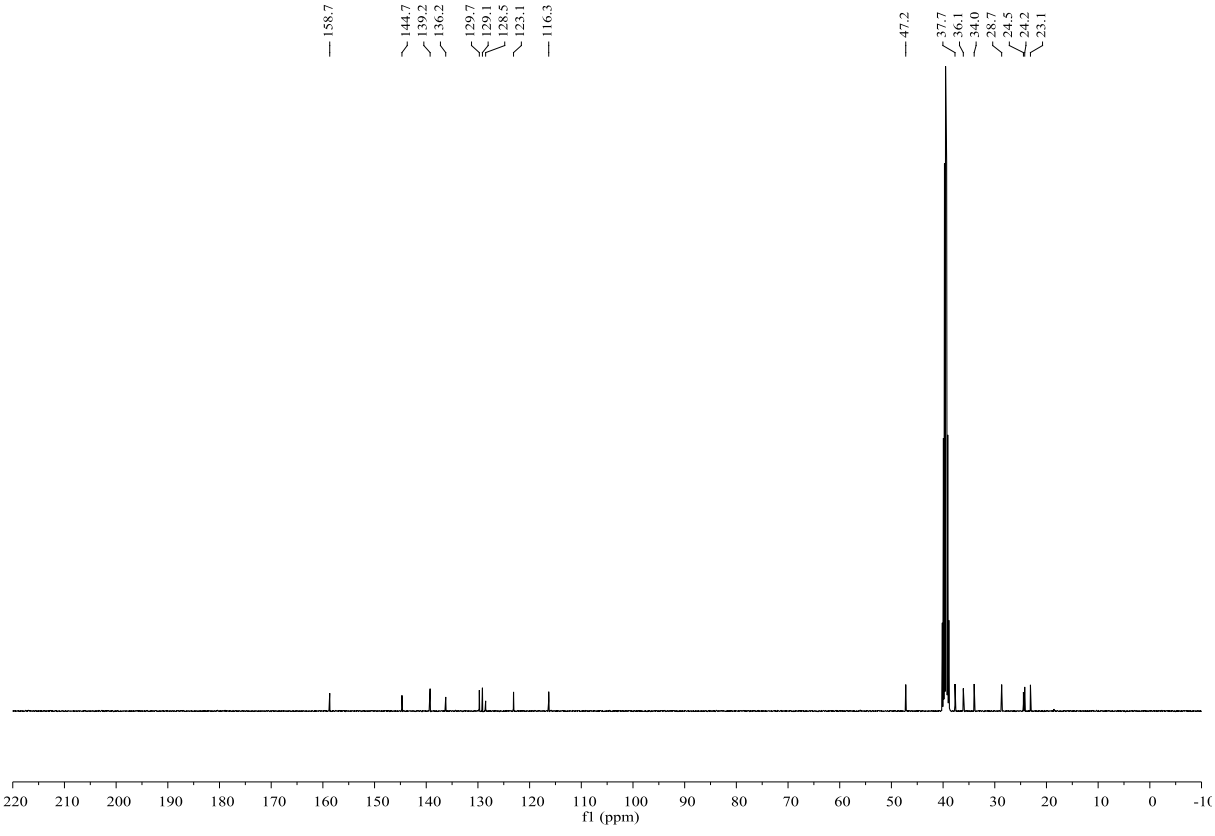


493 (^{1}H NMR, 400 MHz, DMSO-d_6)

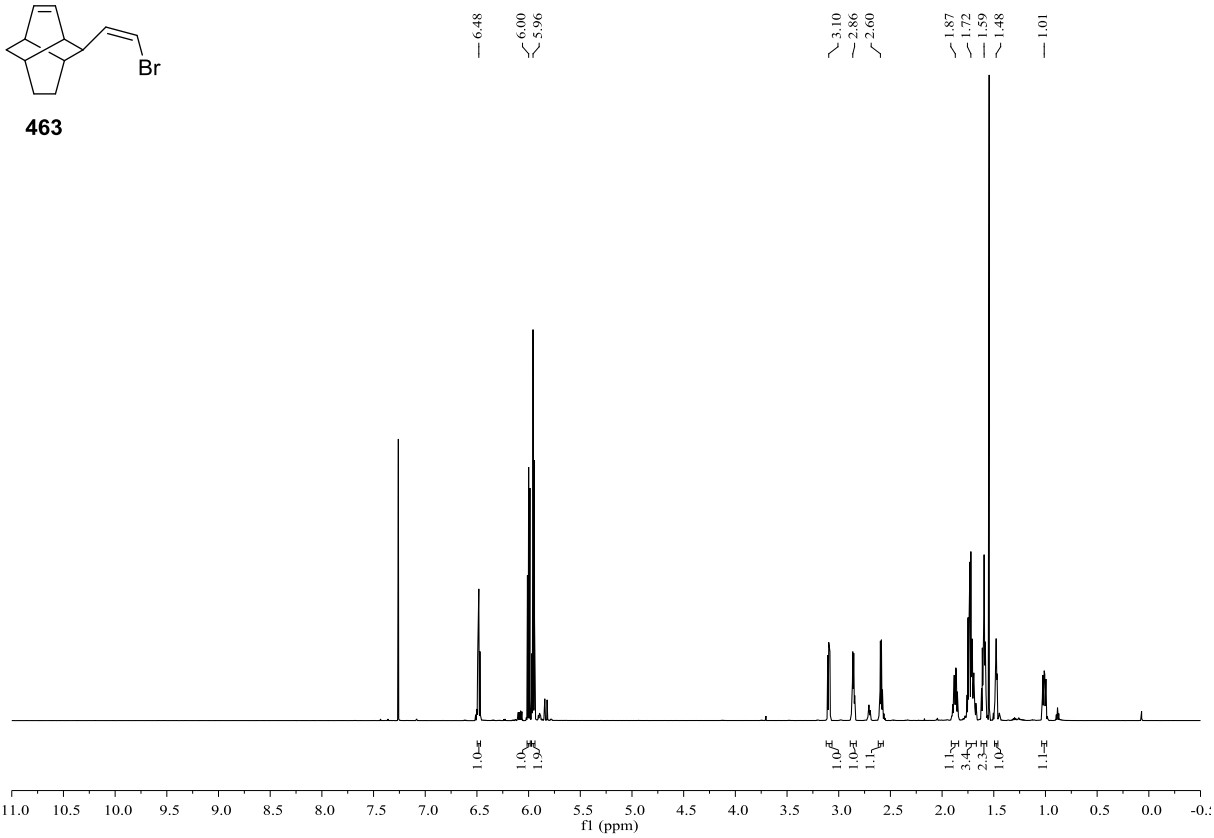


493

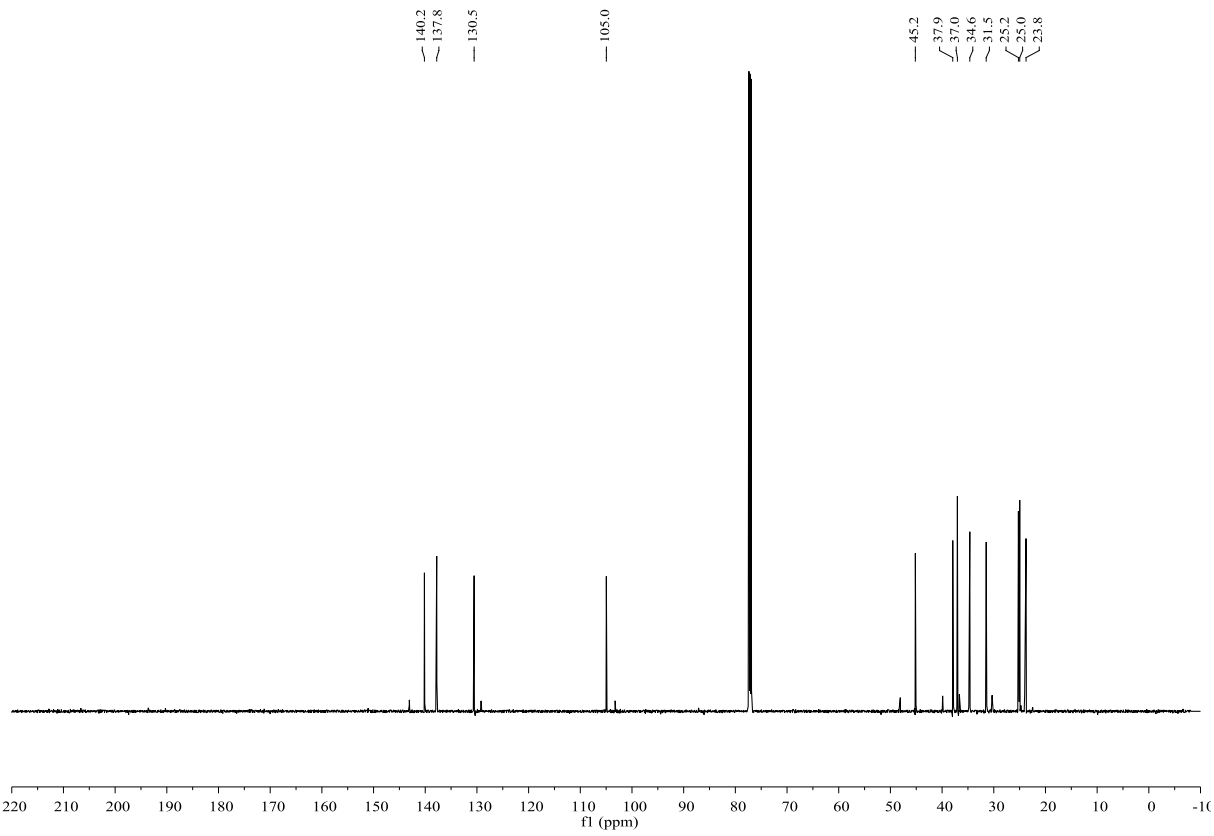
493 (^{13}C NMR, 100 MHz, DMSO-d_6)



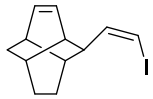
463 (^{1}H NMR, 600 MHz, $CDCl_3$)



463 (^{13}C NMR, 150 MHz, $CDCl_3$)

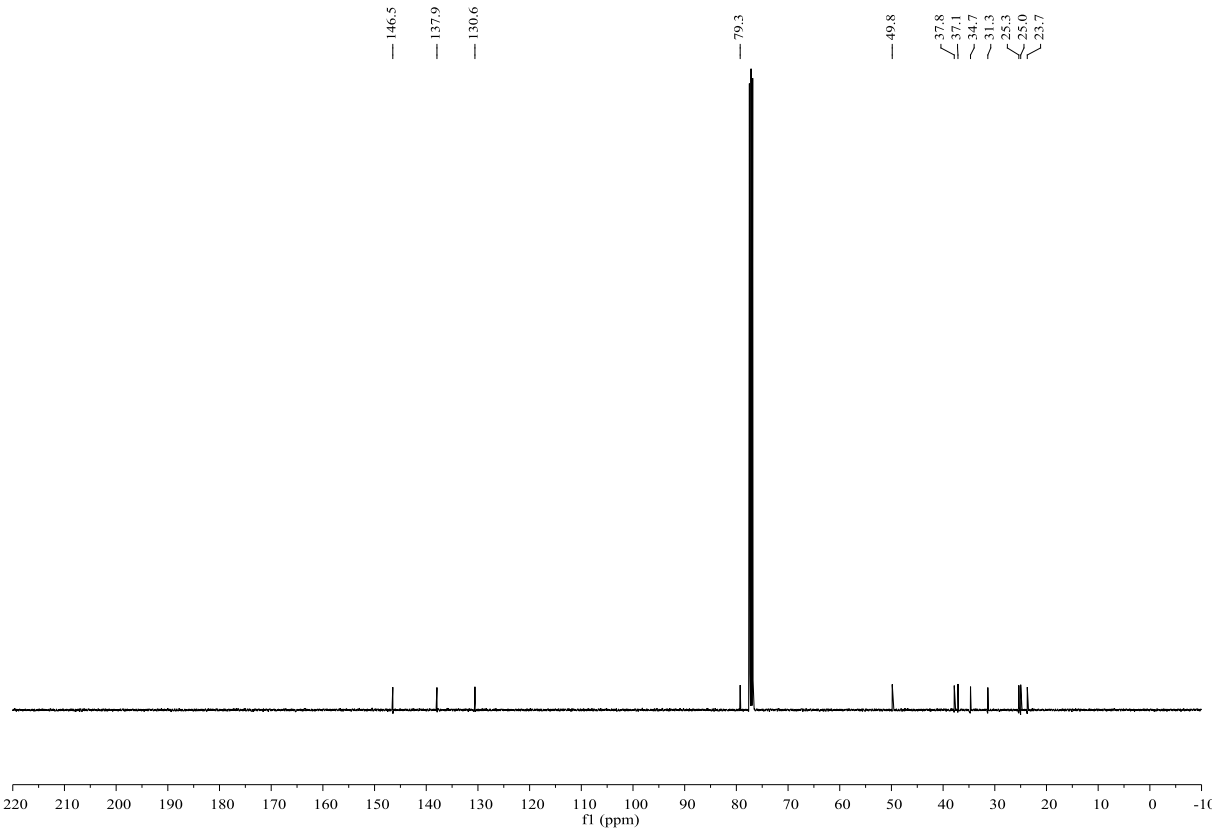


464 (^{1}H NMR, 400 MHz, $CDCl_3$)

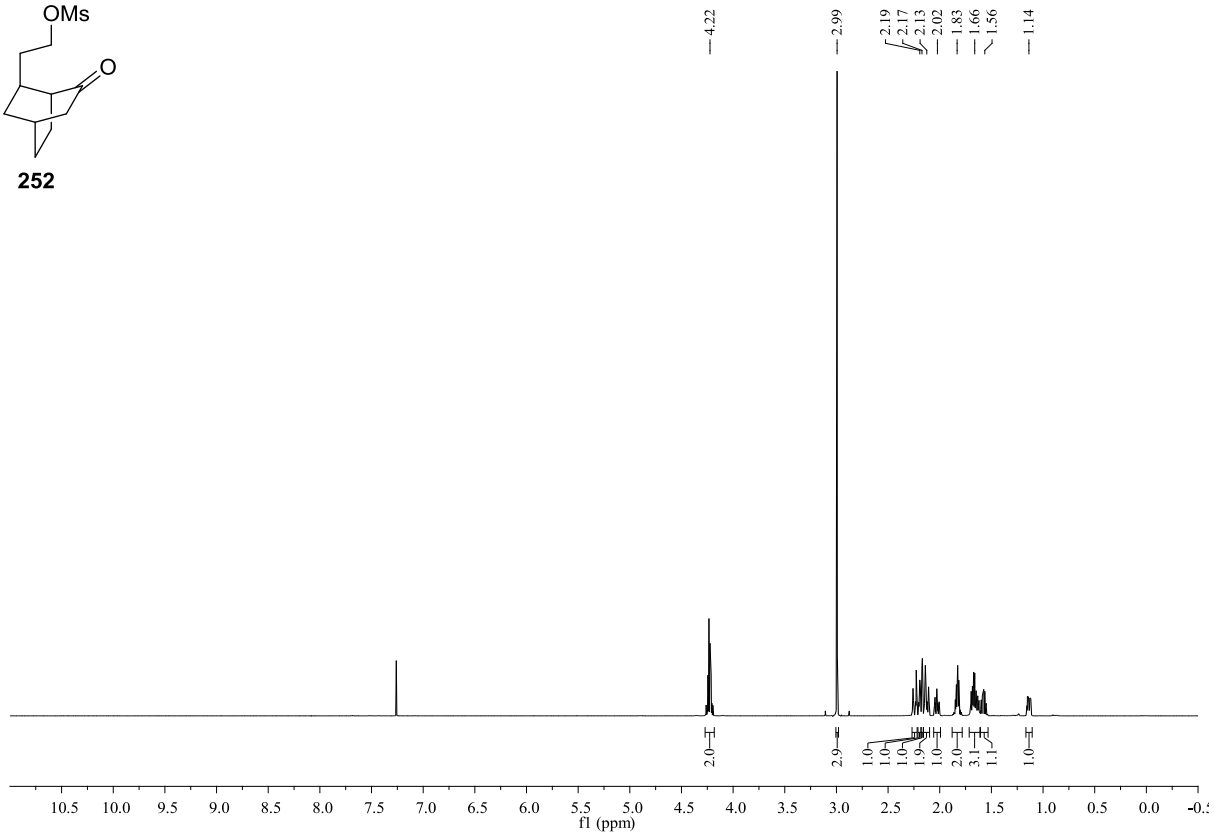


464

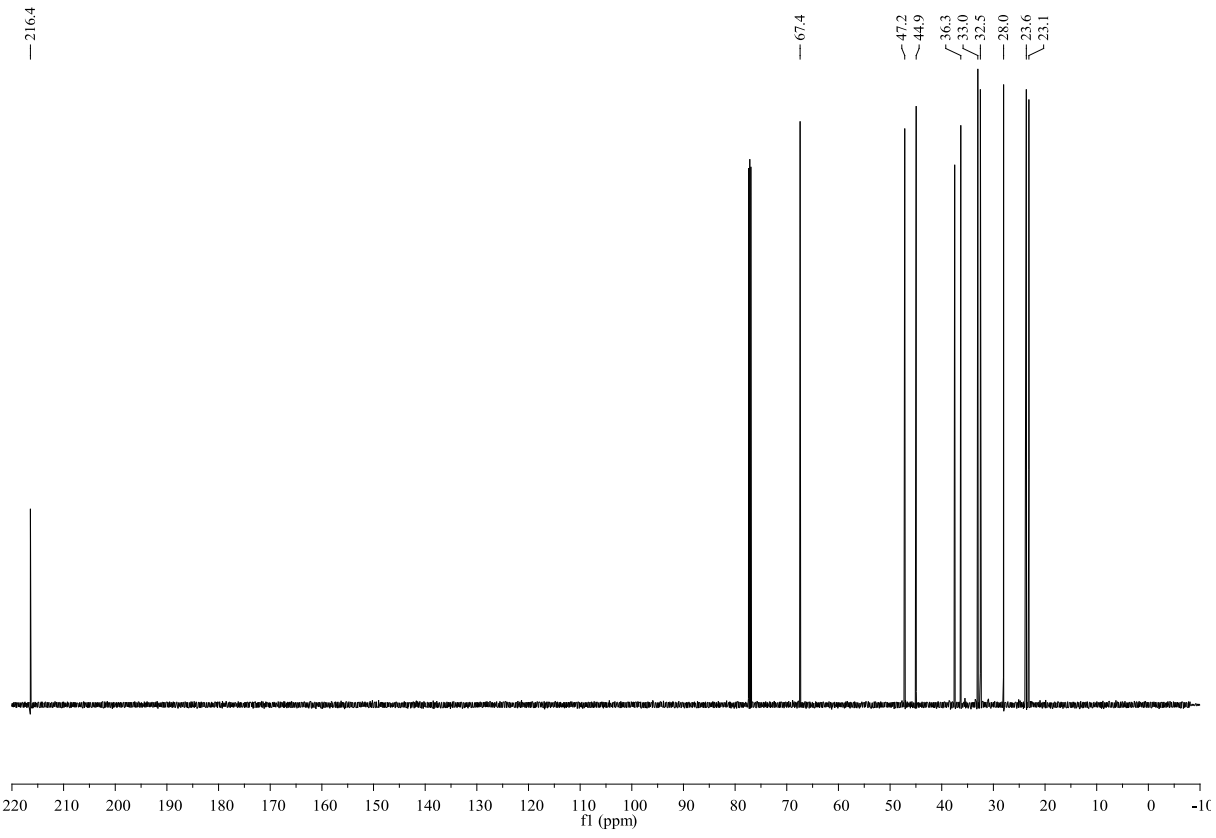
464 (^{13}C NMR, 100 MHz, $CDCl_3$)



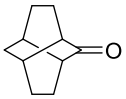
252 (^{1}H NMR, 600 MHz, $CDCl_3$)



252 (^{13}C NMR, 150 MHz, $CDCl_3$)

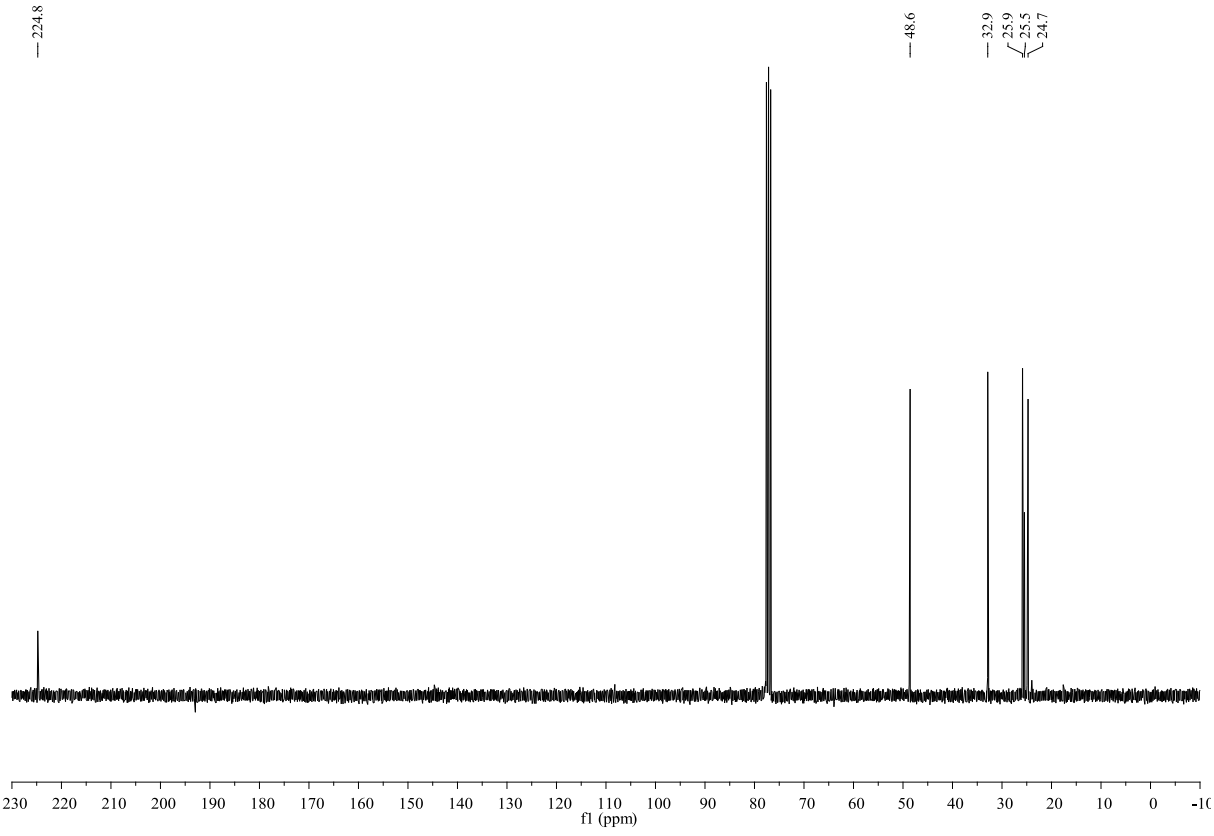


253 (^{1}H NMR, 400 MHz, $CDCl_3$)

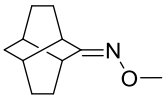


253

253 (^{13}C NMR, 75 MHz, $CDCl_3$)

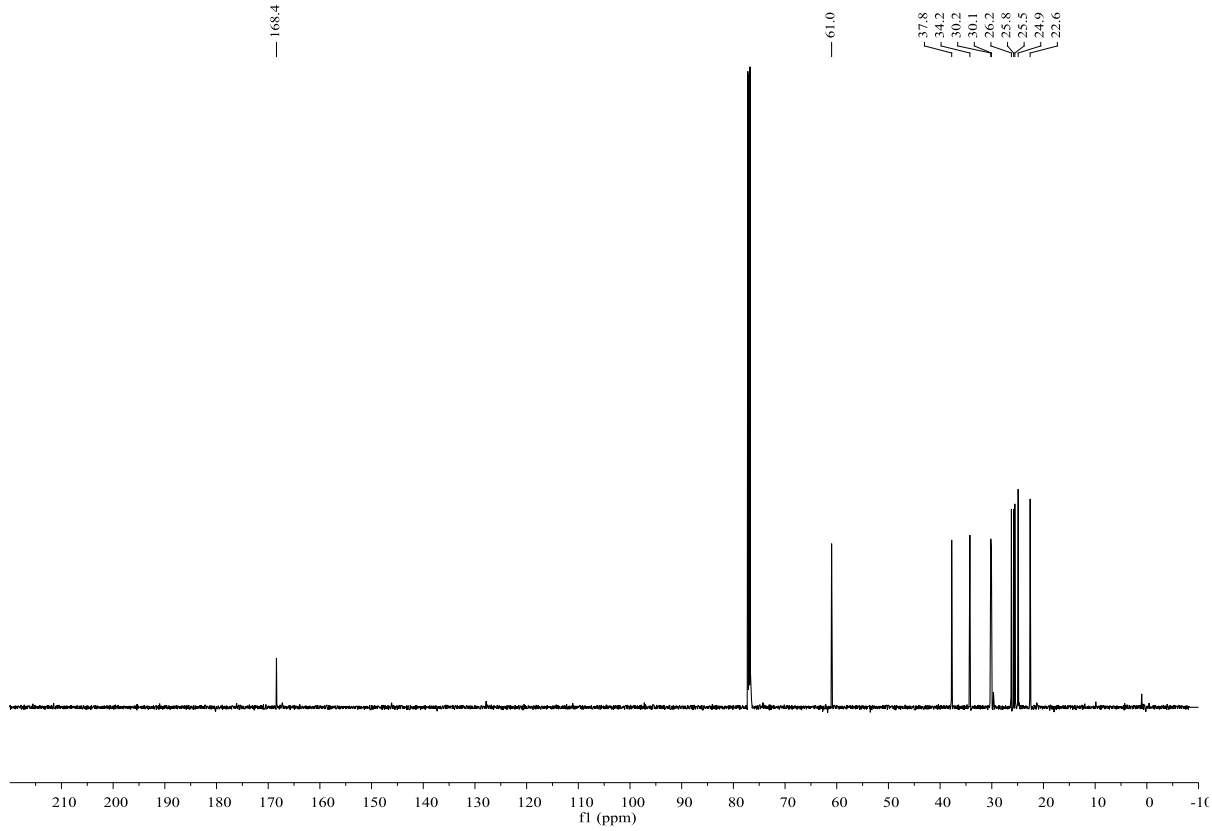


494 (^{1}H NMR, 600 MHz, $CDCl_3$)

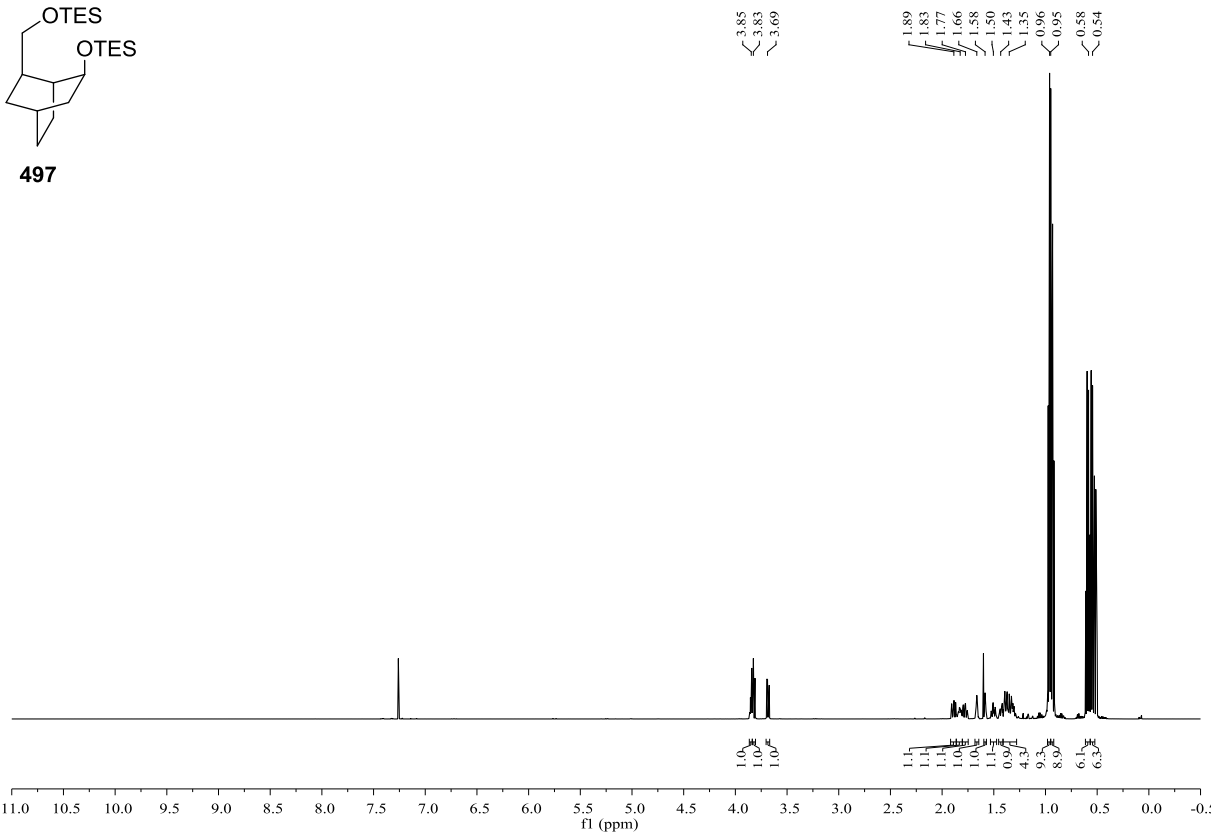


494

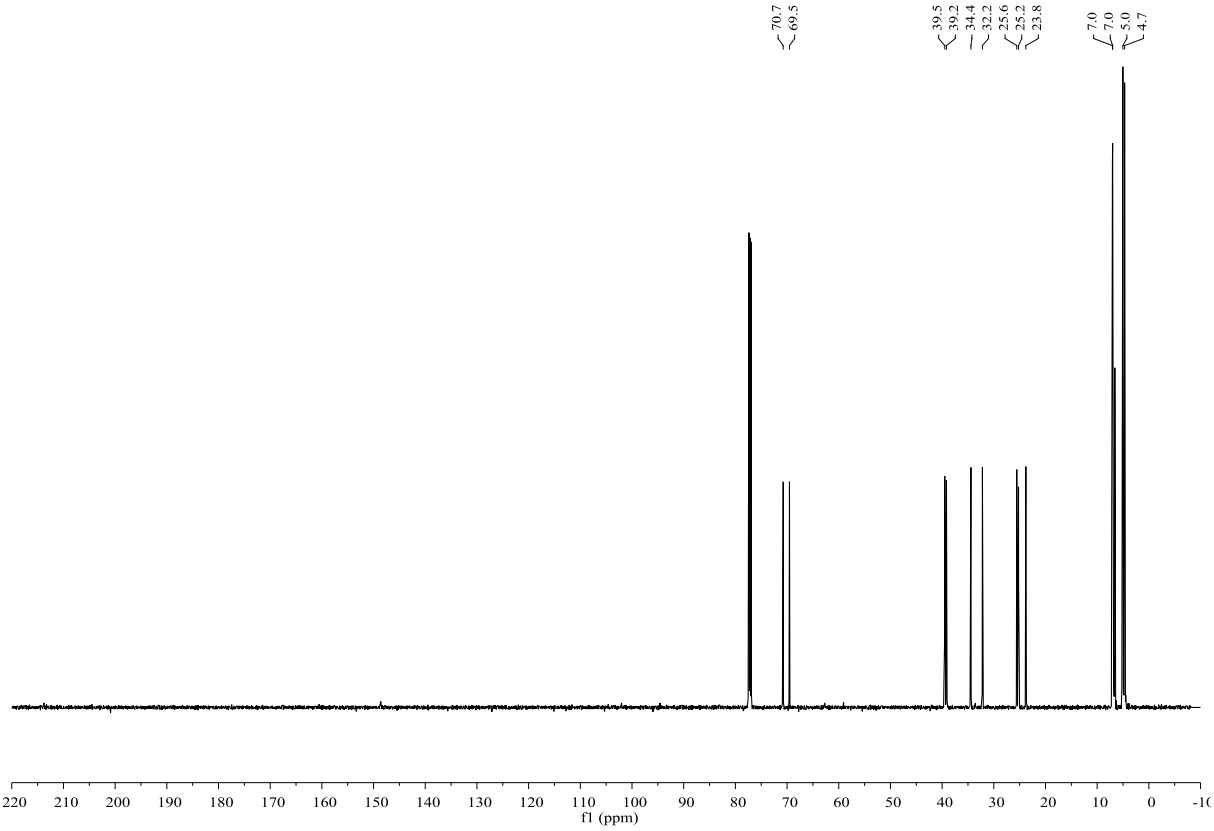
494 (^{13}C NMR, 150 MHz, $CDCl_3$)



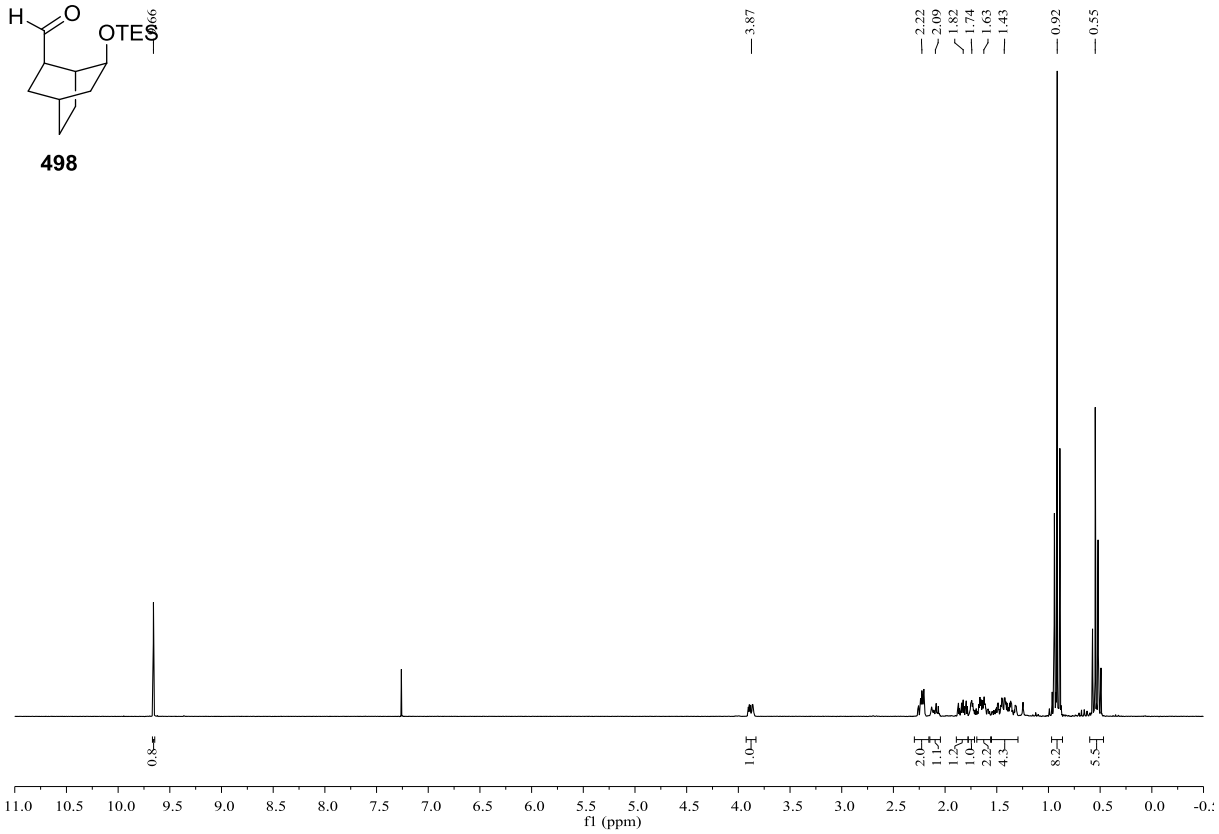
497 (^{1}H NMR, 600 MHz, $CDCl_3$)



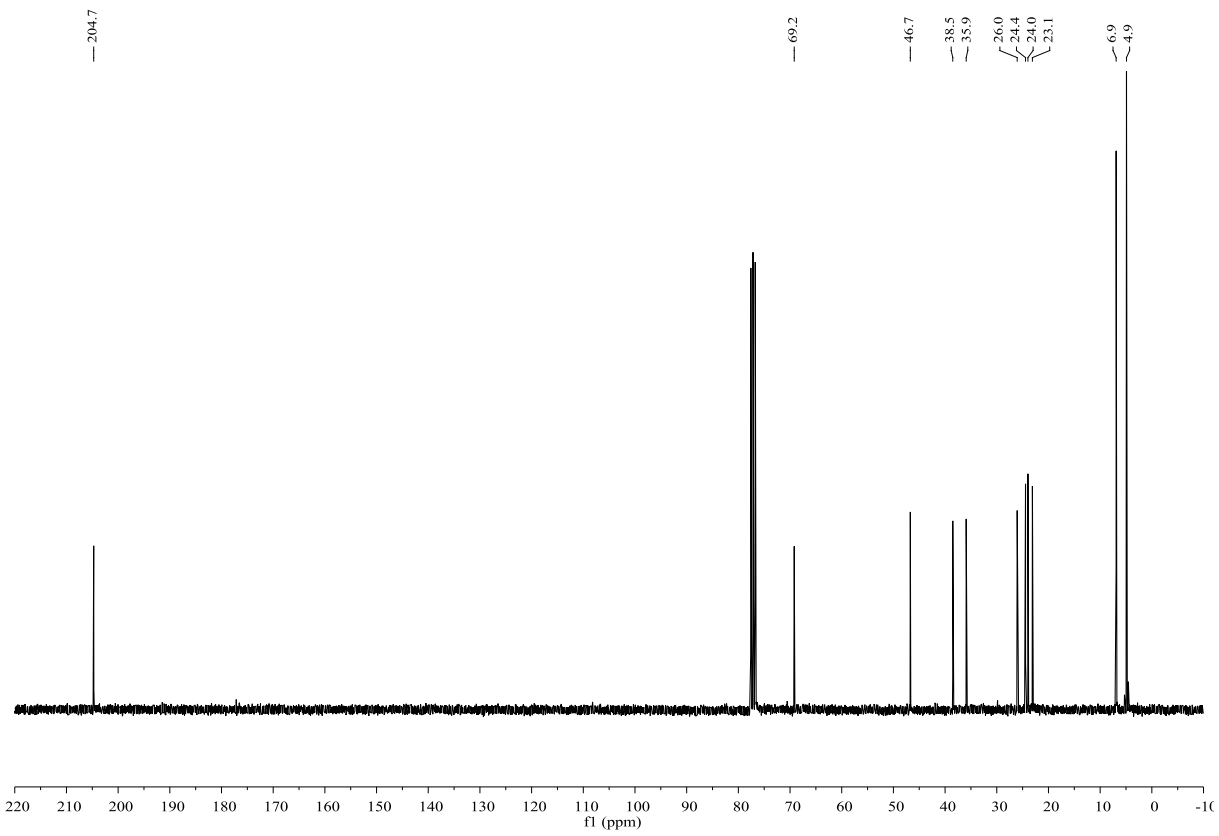
497 (^{13}C NMR, 150 MHz, $CDCl_3$)



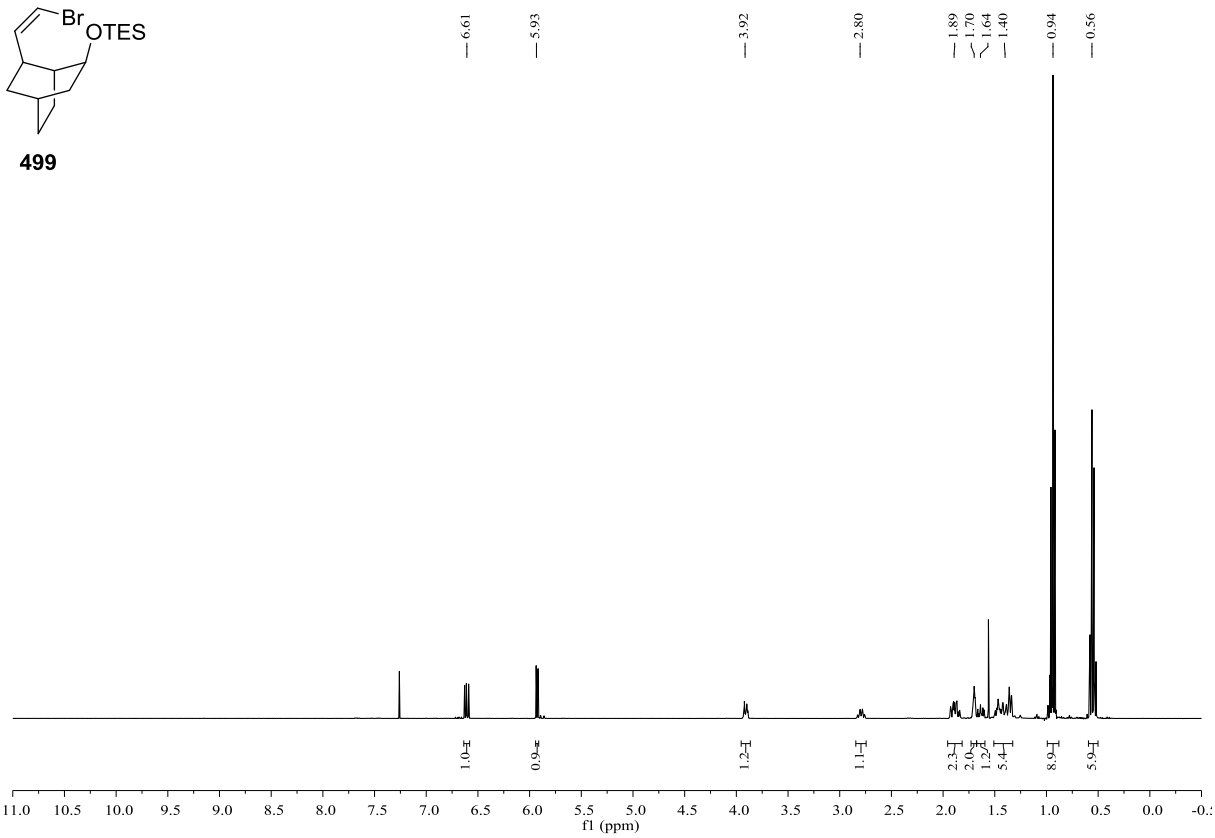
498 (^{1}H NMR, 300 MHz, $CDCl_3$)



498 (^{13}C NMR, 75 MHz, $CDCl_3$)

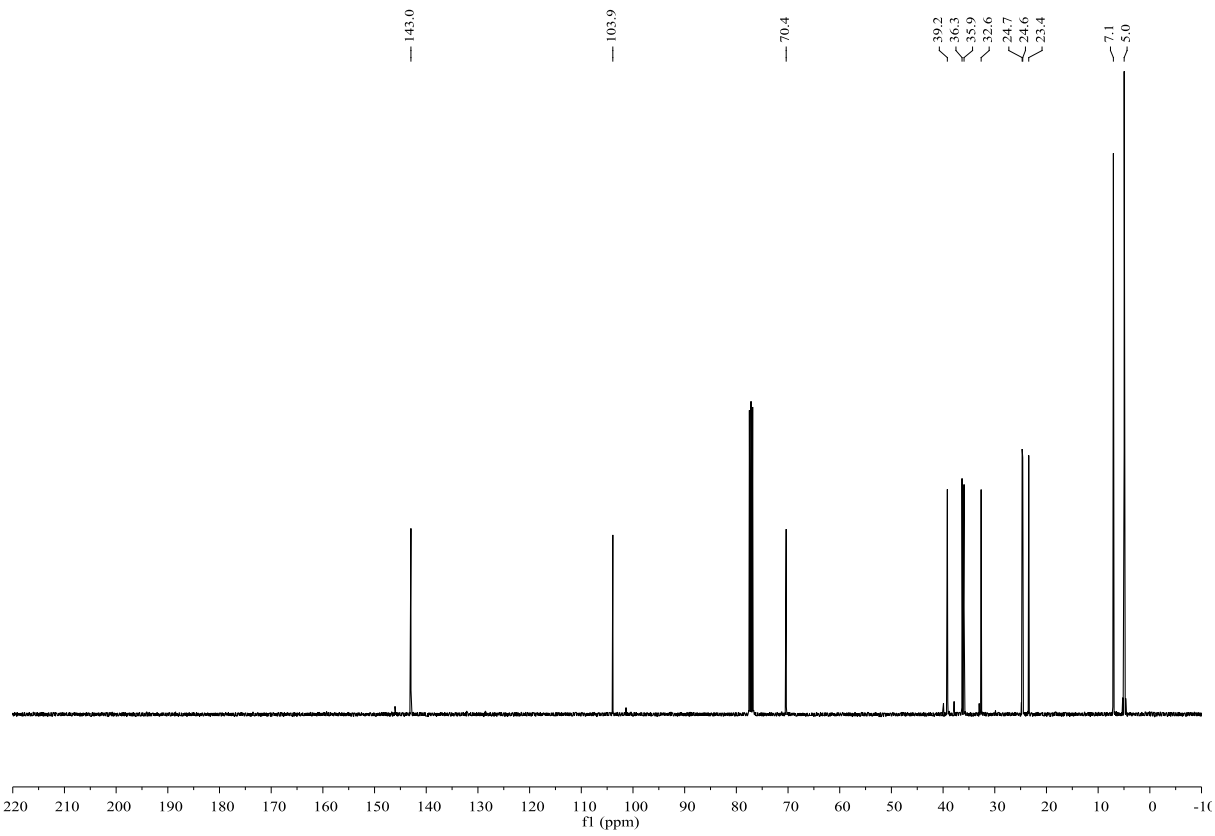


499 (^{1}H NMR, 400 MHz, $CDCl_3$)

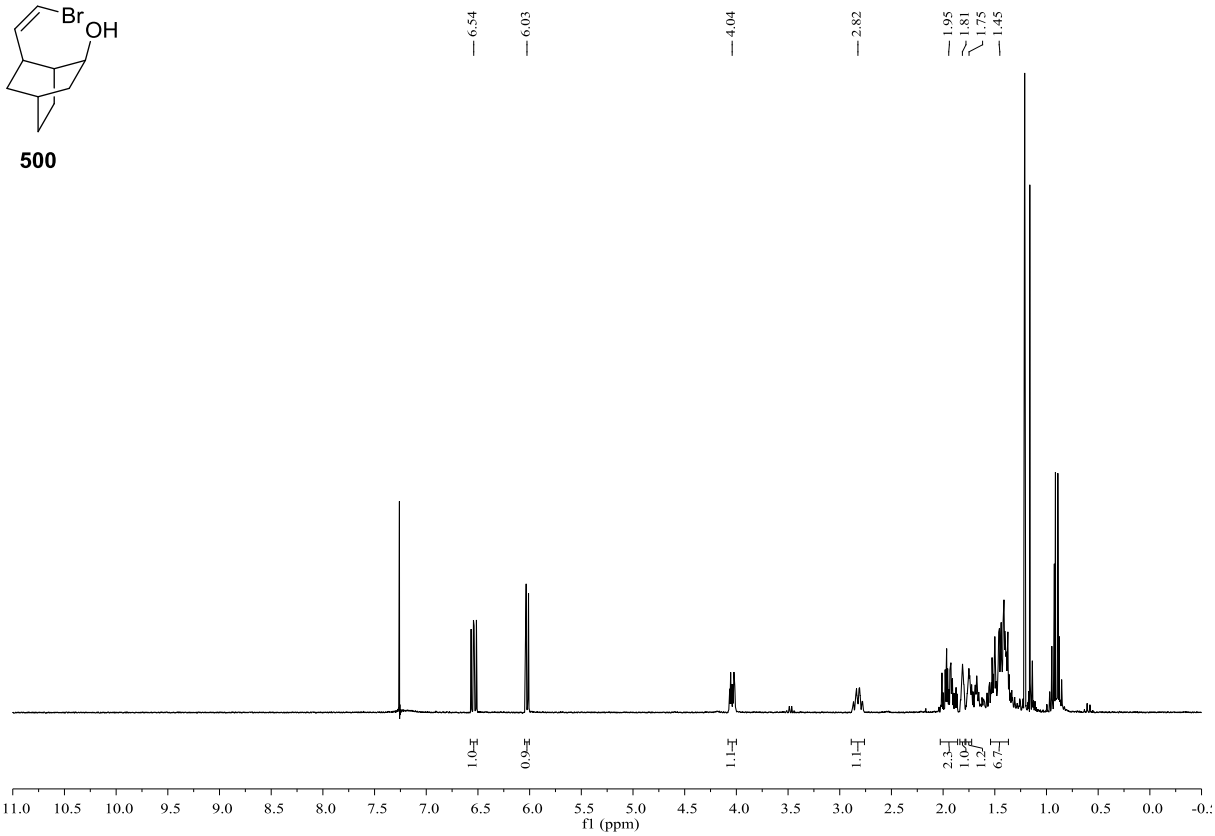


499

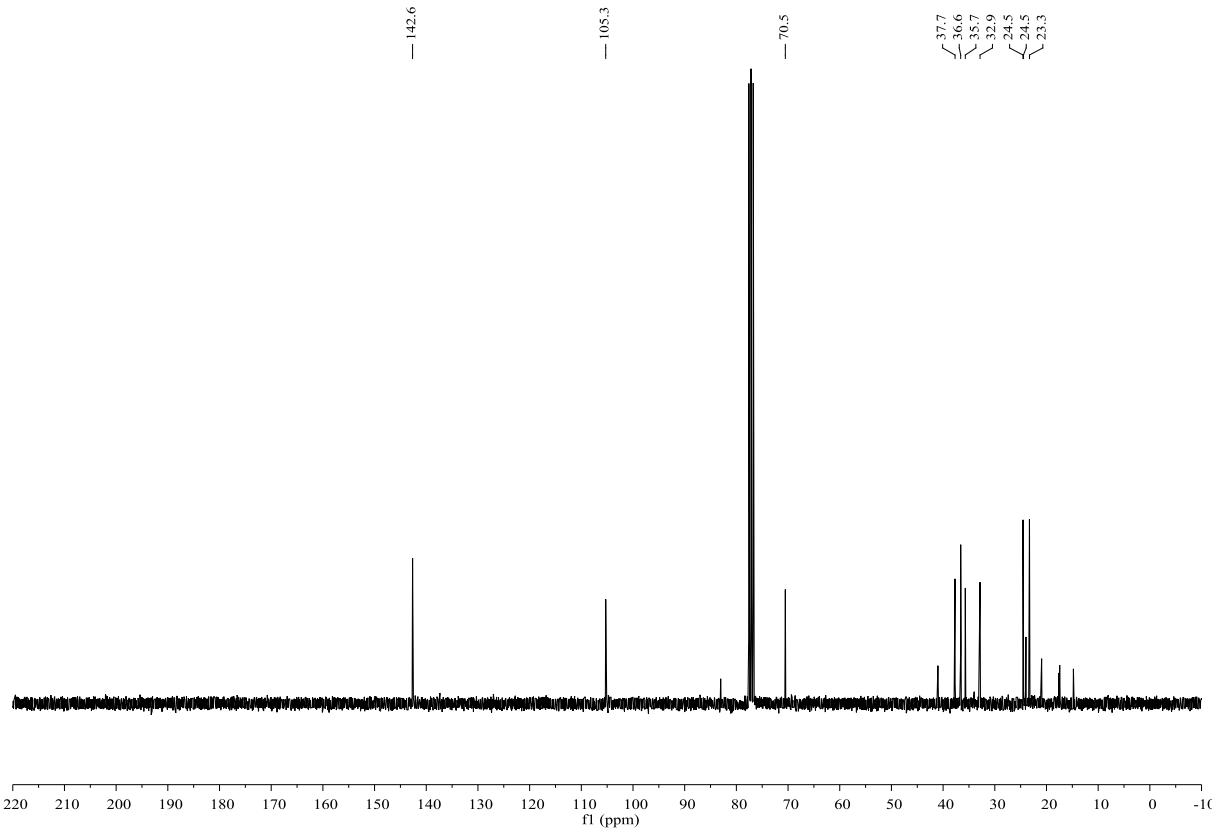
499 (^{13}C NMR, 100 MHz, $CDCl_3$)



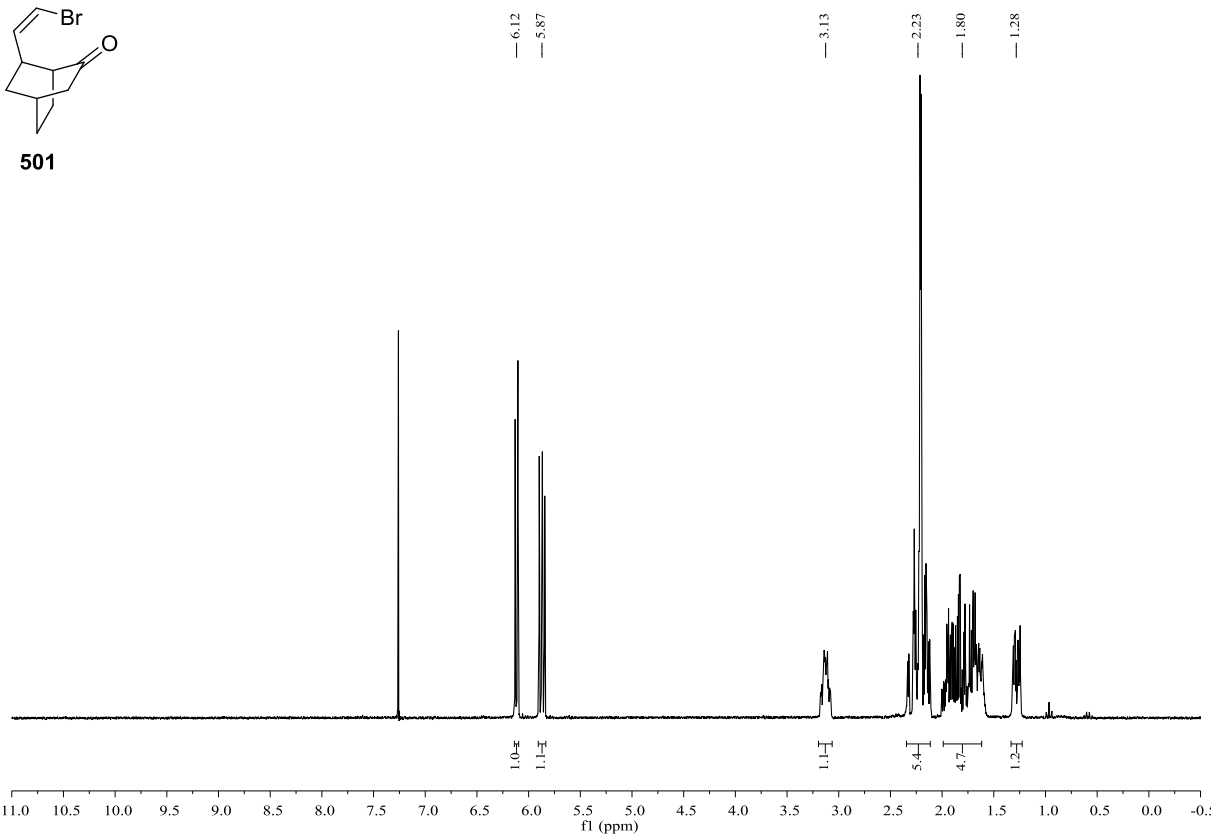
500 (^{1}H NMR, 300 MHz, $CDCl_3$)



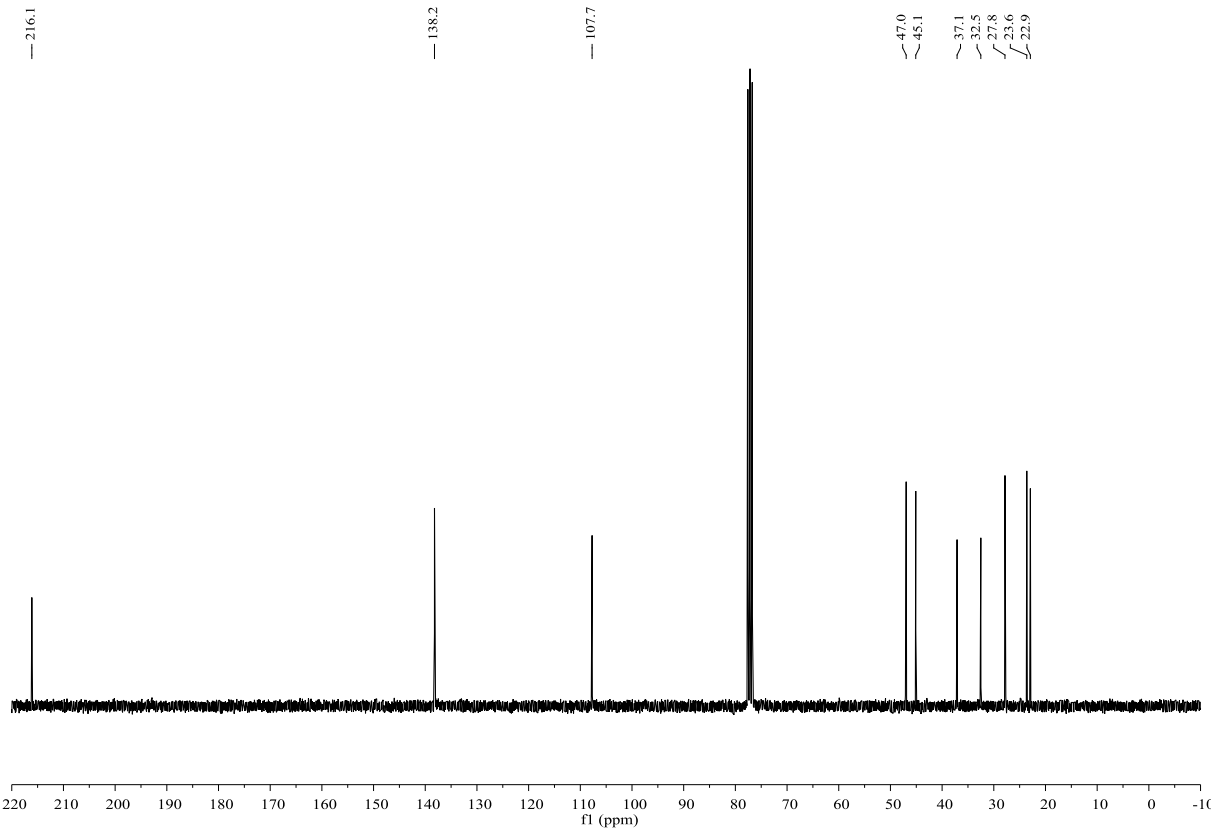
500 (^{13}C NMR, 75 MHz, $CDCl_3$)



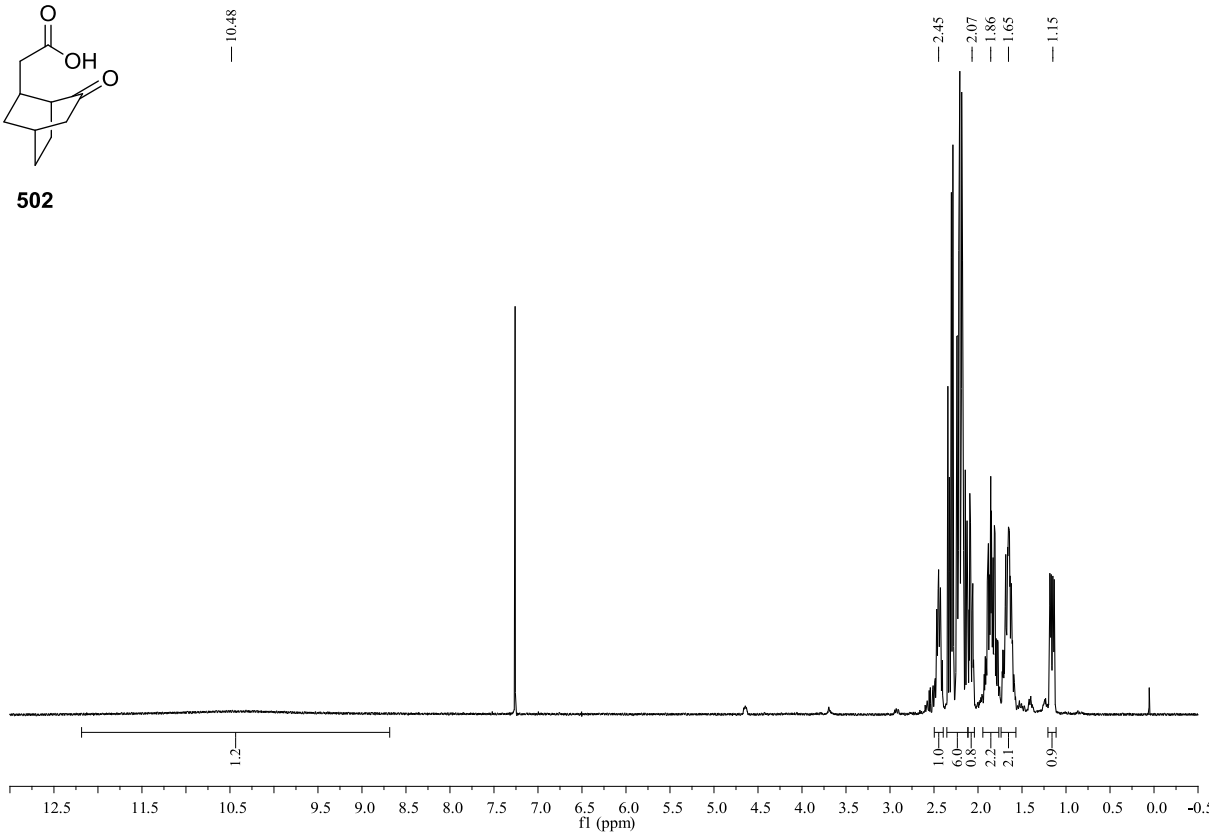
501 (^{1}H NMR, 300 MHz, $CDCl_3$)



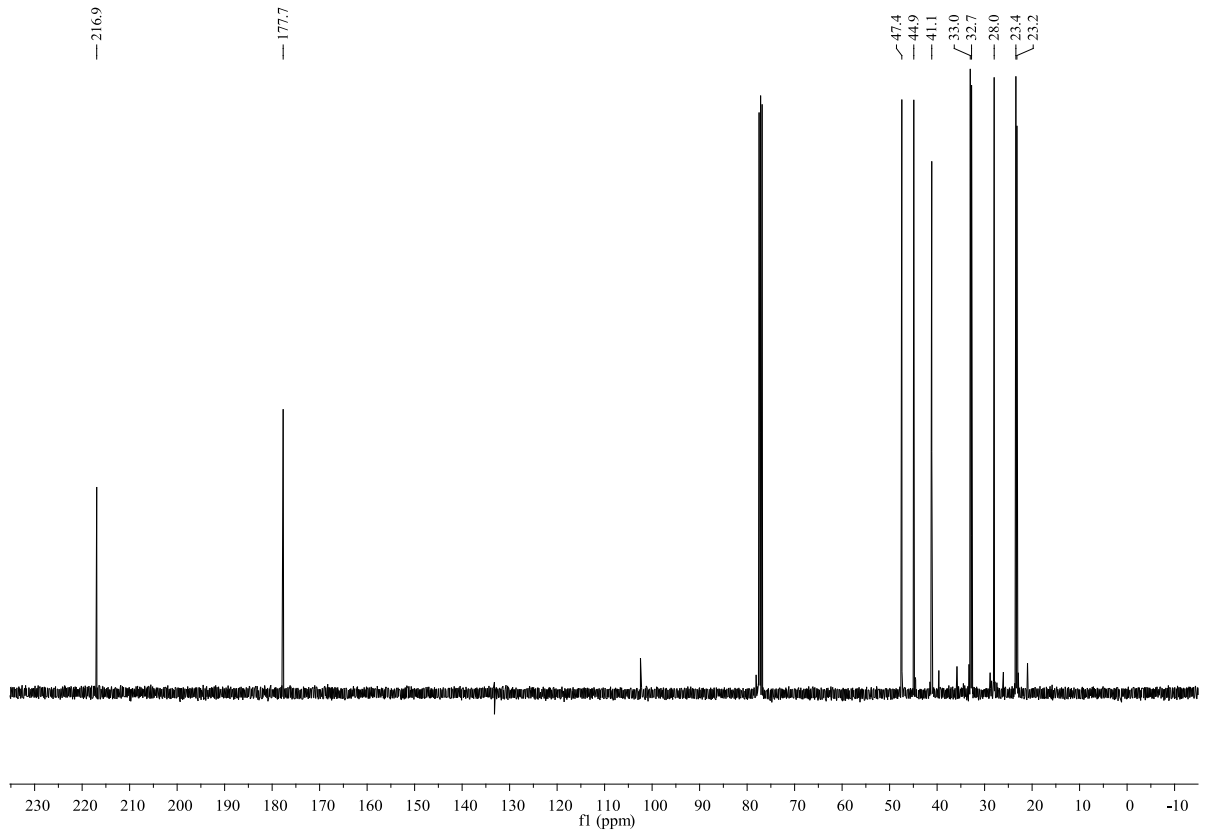
501 (^{13}C NMR, 75 MHz, $CDCl_3$)



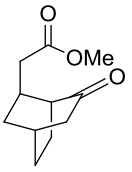
502 (^{1}H NMR, 400 MHz, $CDCl_3$)



502 (^{13}C NMR, 100 MHz, $CDCl_3$)

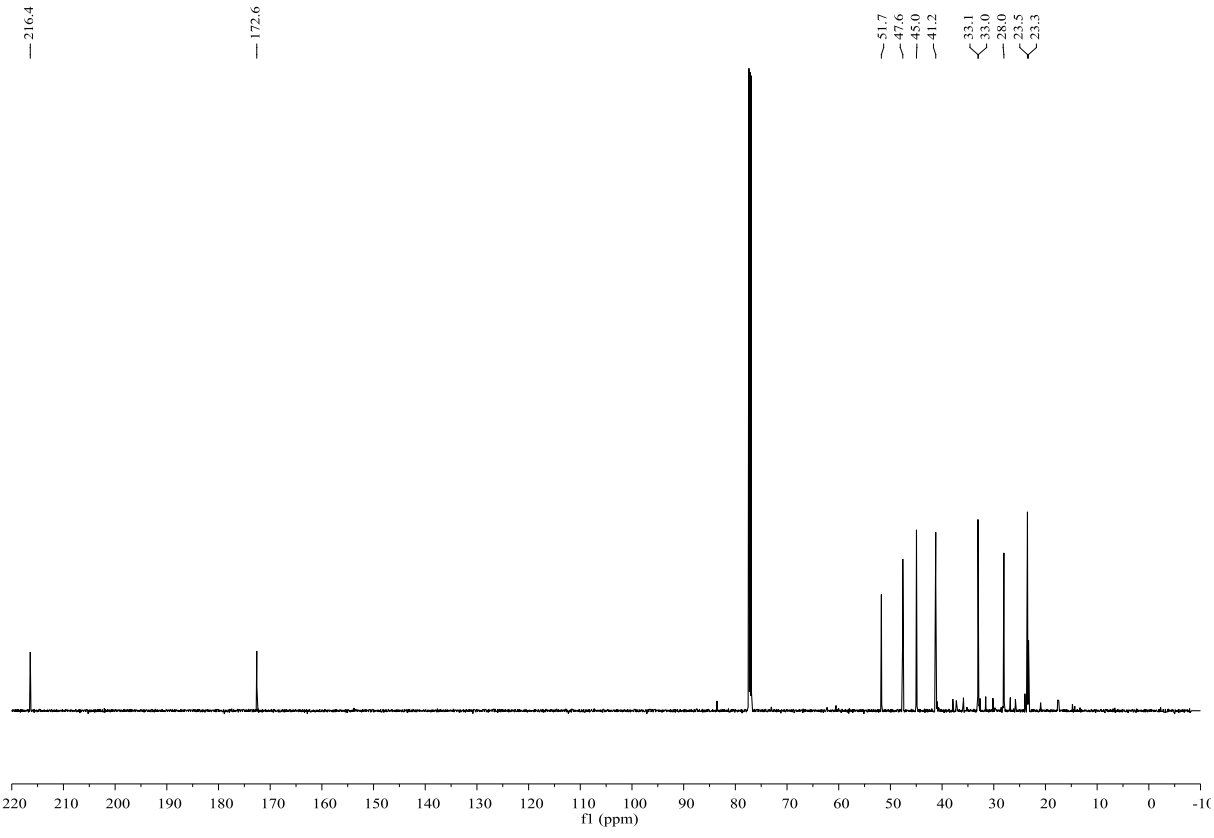


503 (^{1}H NMR, 600 MHz, $CDCl_3$)

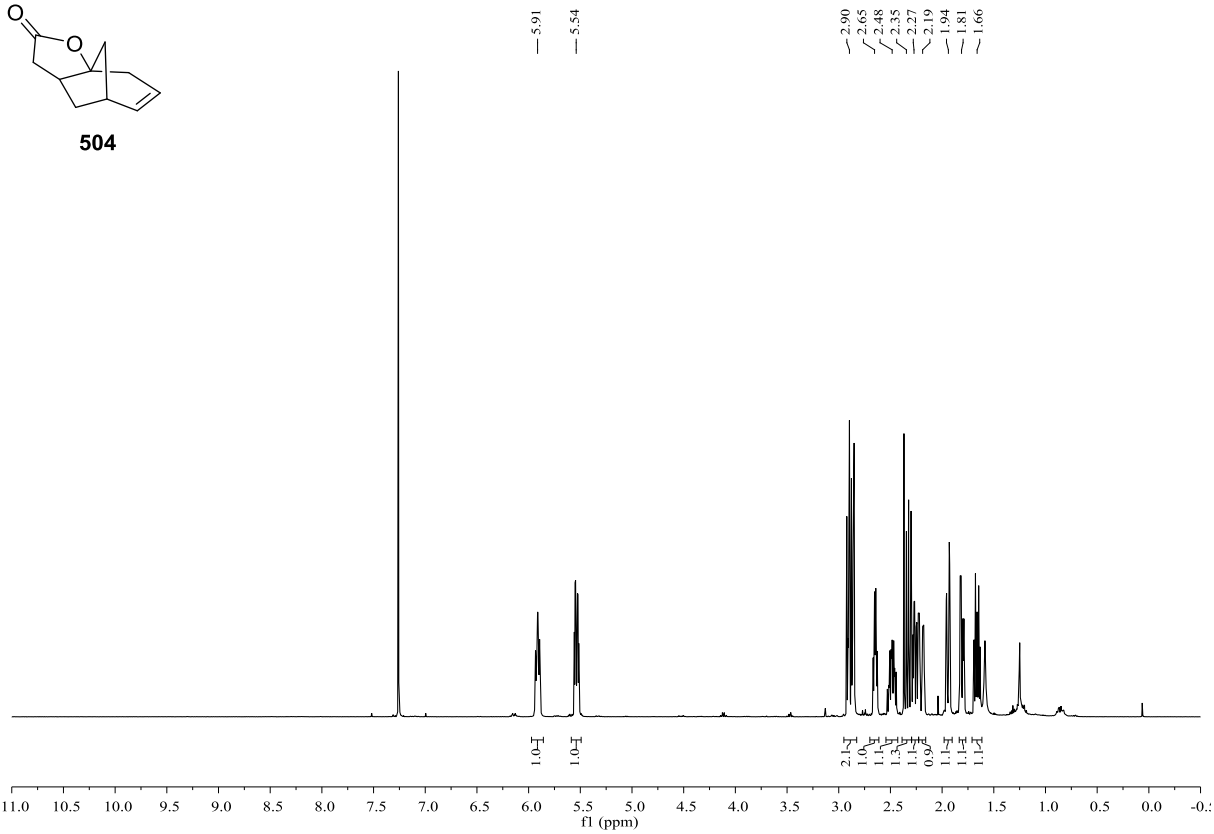


503

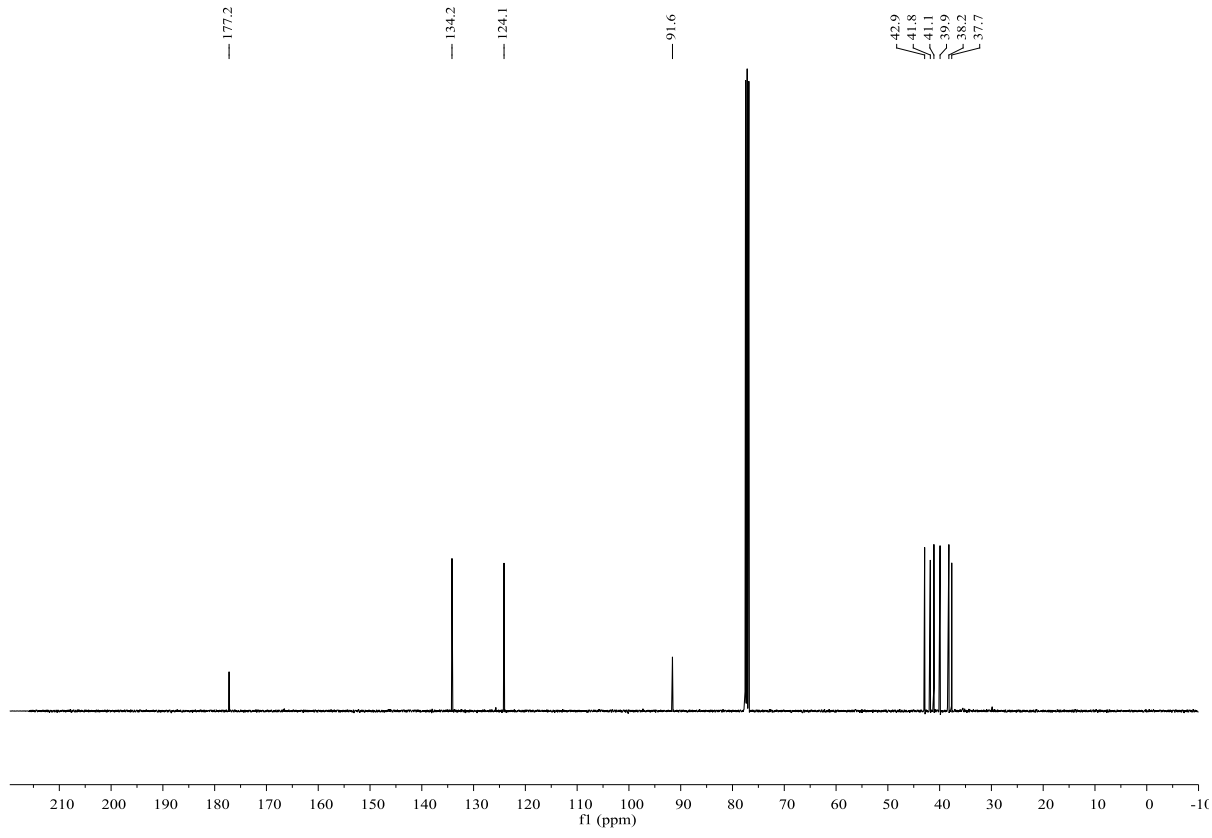
503 (^{13}C NMR, 150 MHz, $CDCl_3$)



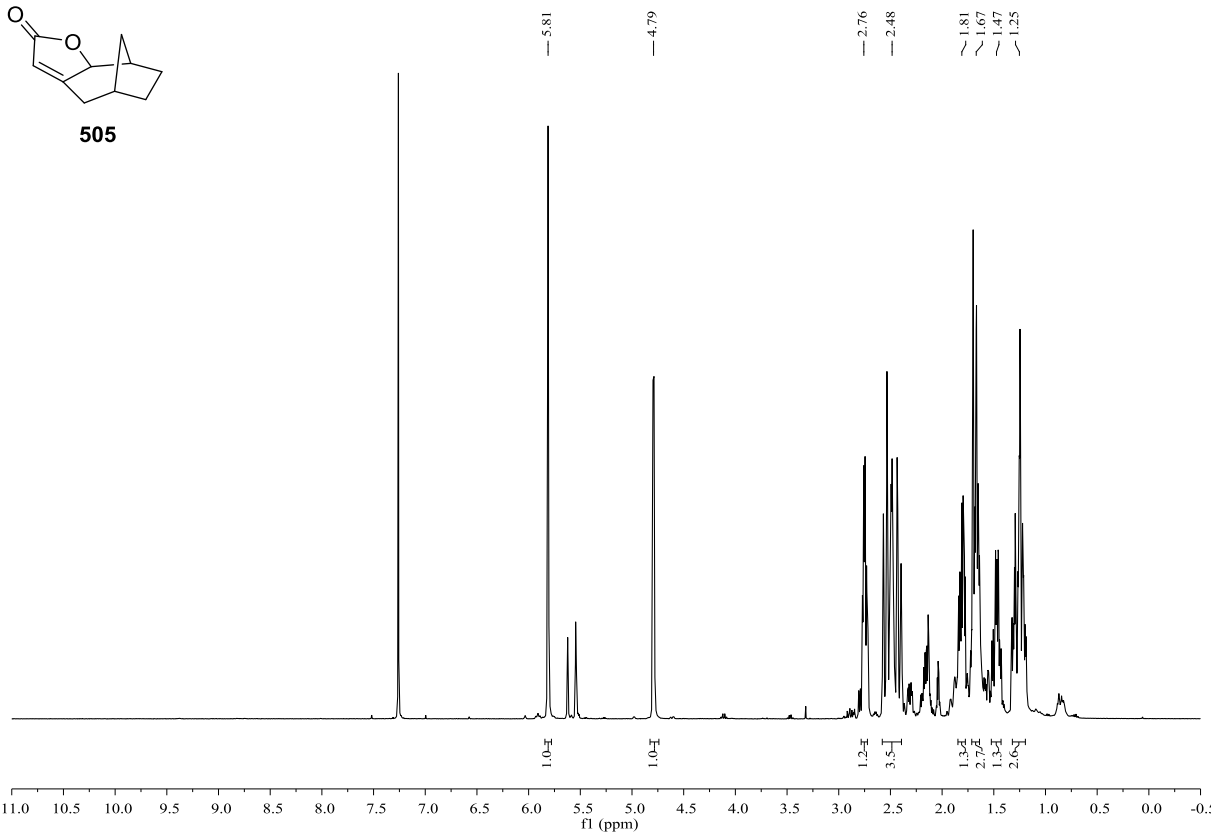
504 (^{1}H NMR, 400 MHz, $CDCl_3$)



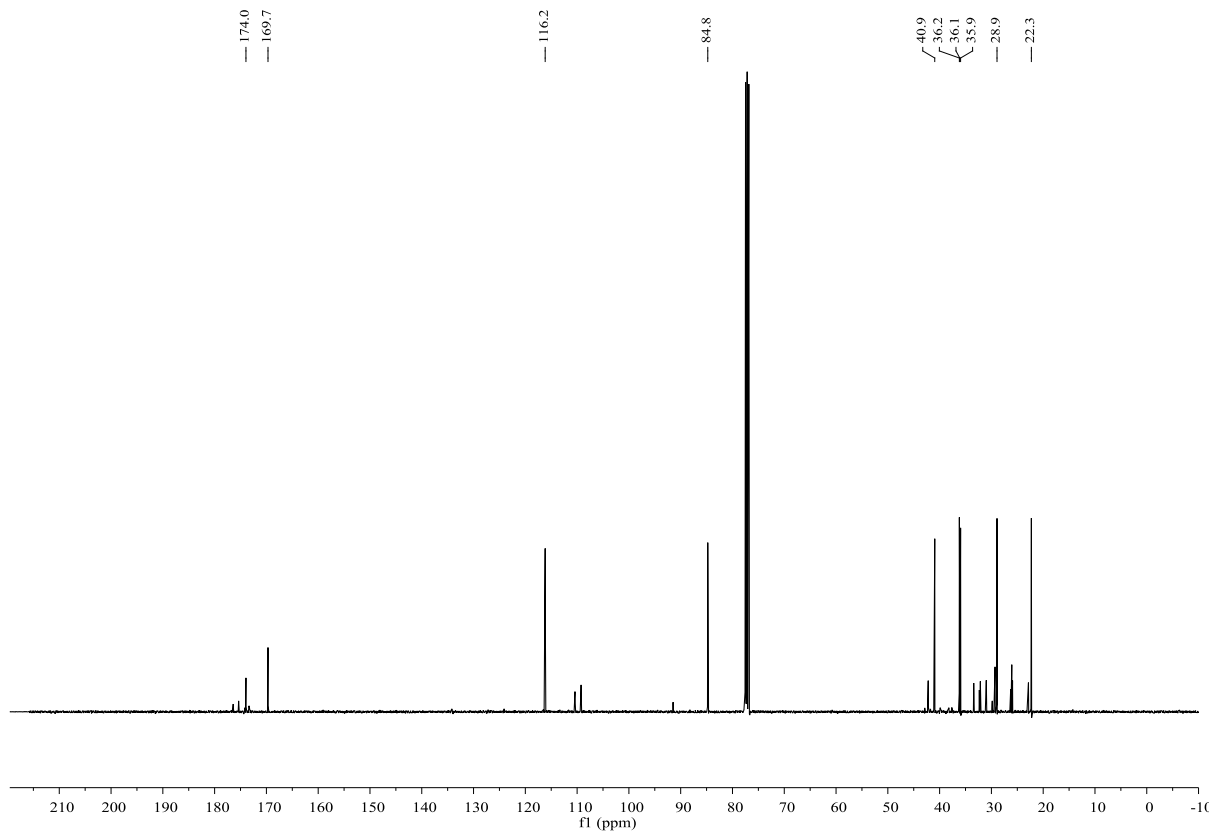
504 (^{13}C NMR, 100 MHz, $CDCl_3$)



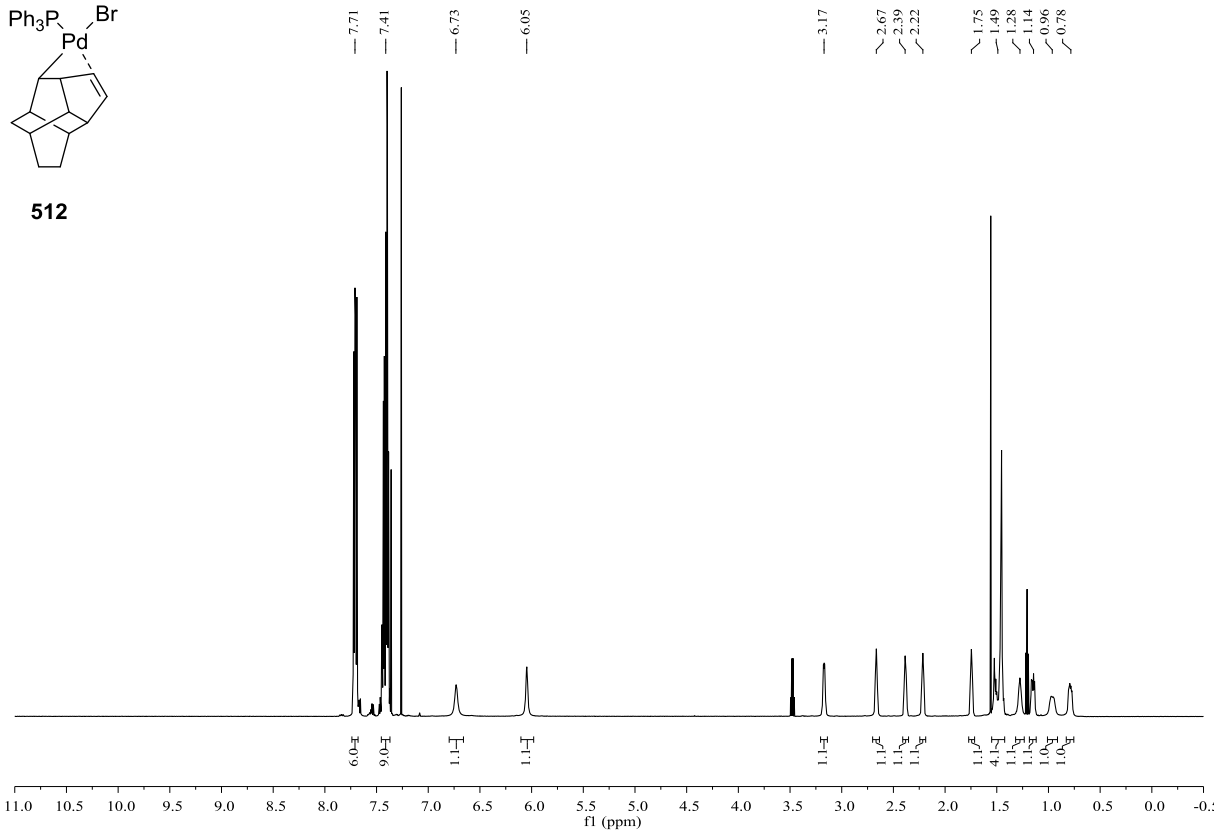
505 (^{1}H NMR, 400 MHz, $CDCl_3$)



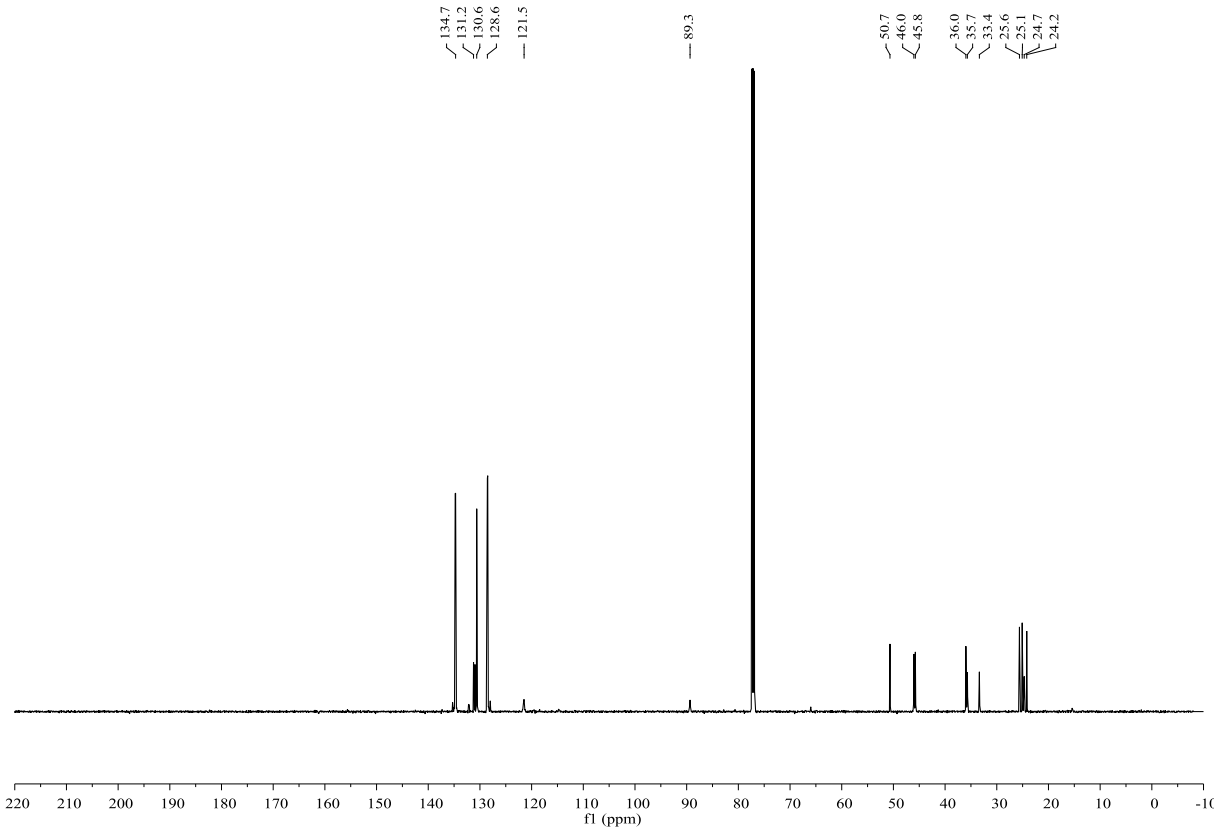
505 (^{13}C NMR, 100 MHz, $CDCl_3$)



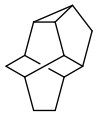
512 (^{1}H NMR, 600 MHz, $CDCl_3$)



512 (^{13}C NMR, 150 MHz, $CDCl_3$)

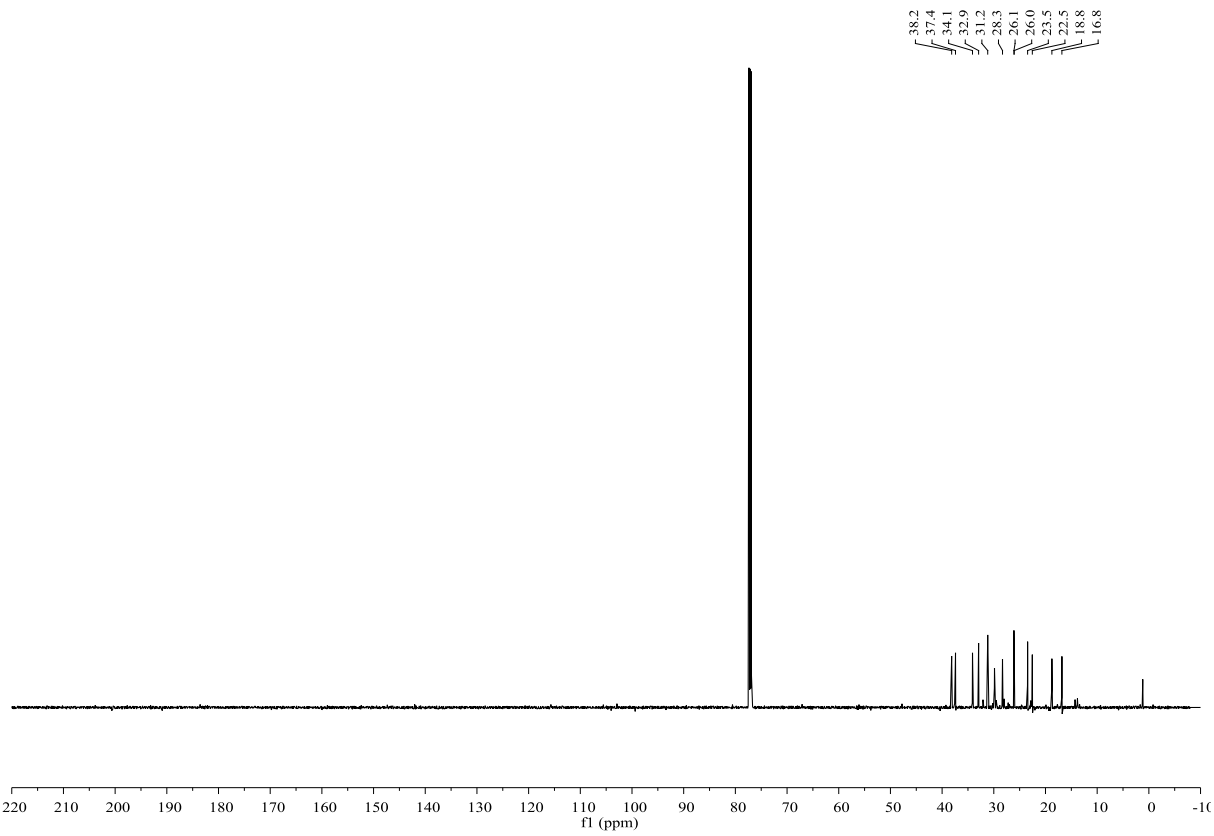


465 (^{1}H NMR, 600 MHz, $CDCl_3$)

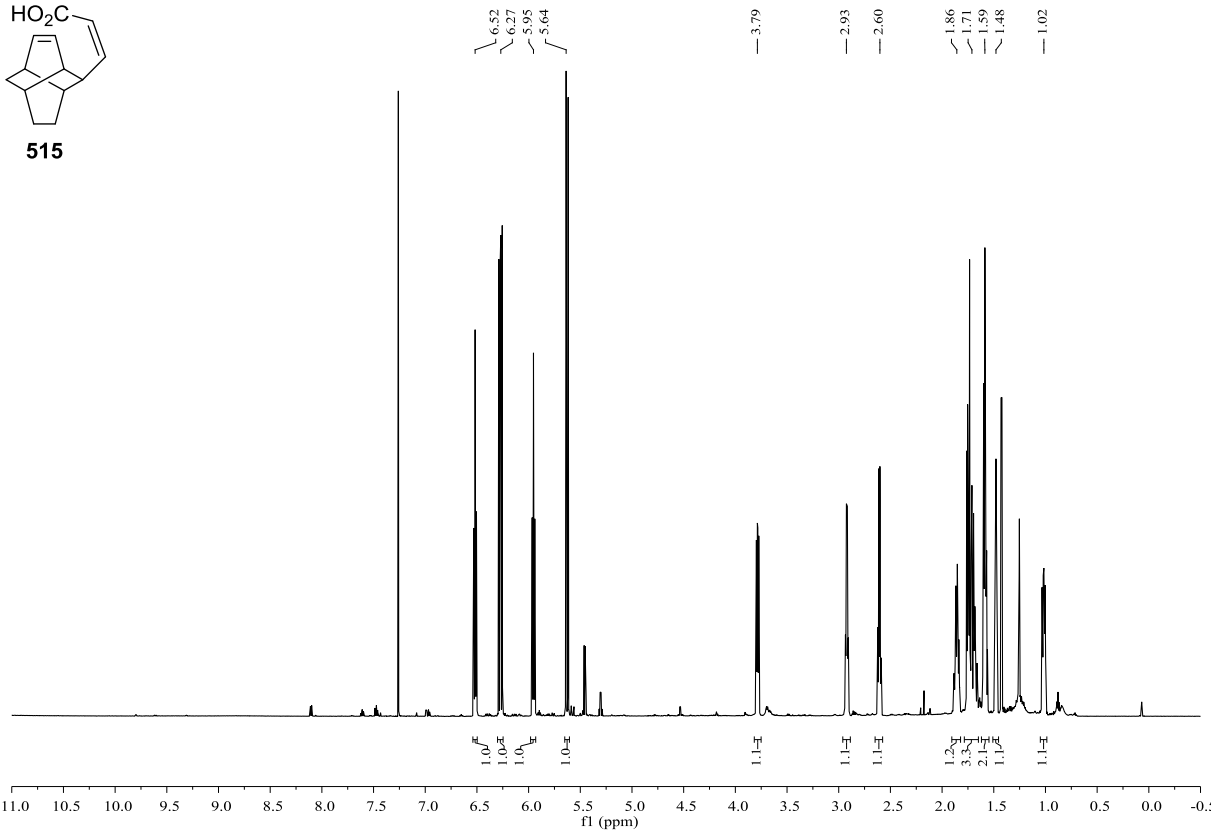


465

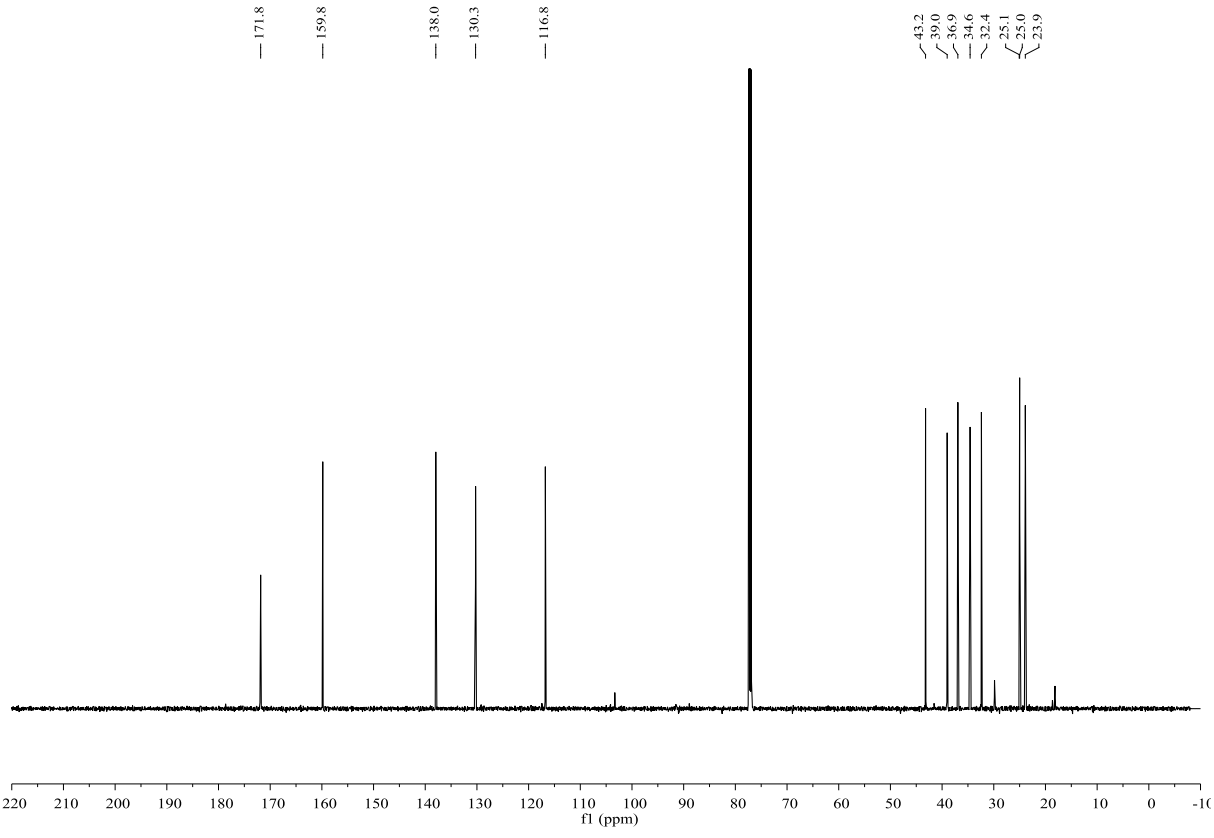
465 (^{13}C NMR, 150 MHz, $CDCl_3$)



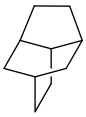
515 (^{1}H NMR, 600 MHz, $CDCl_3$)



515 (^{13}C NMR, 150 MHz, $CDCl_3$)

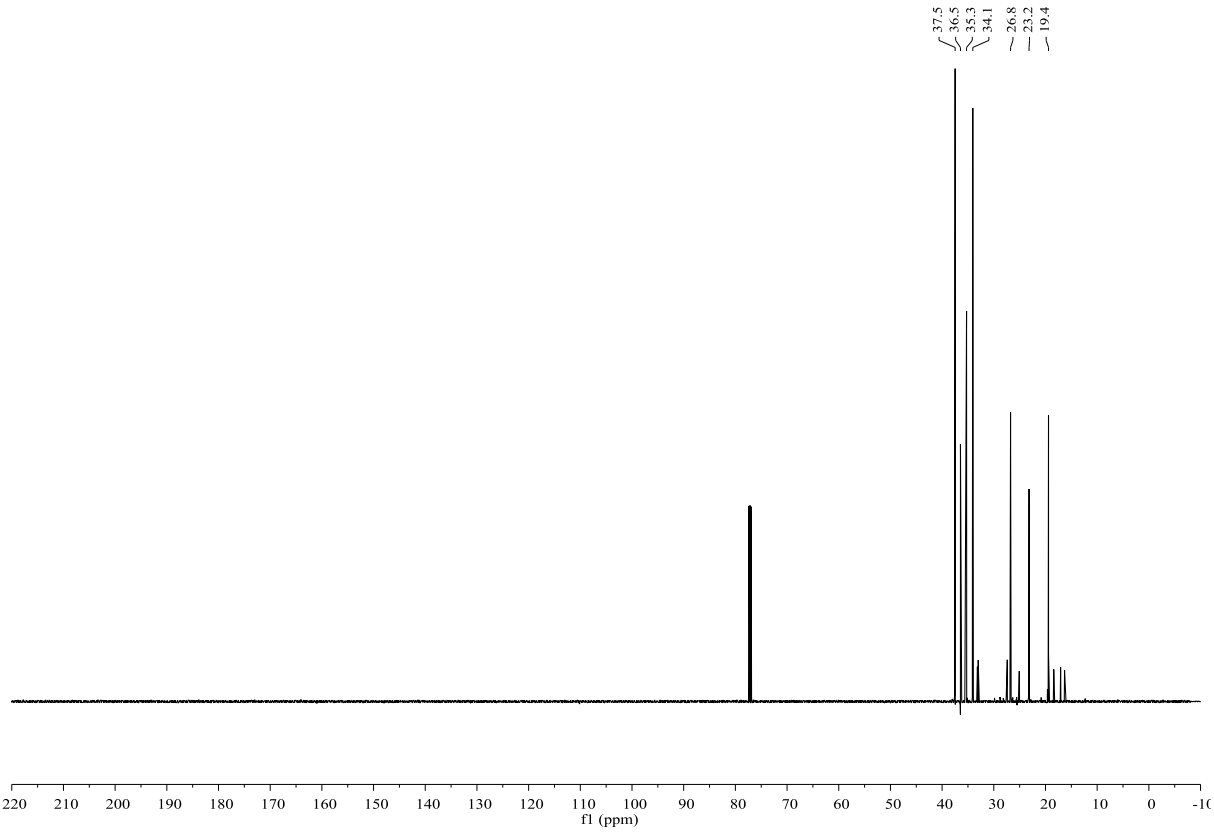


544 (^{1}H NMR, 600 MHz, $CDCl_3$)

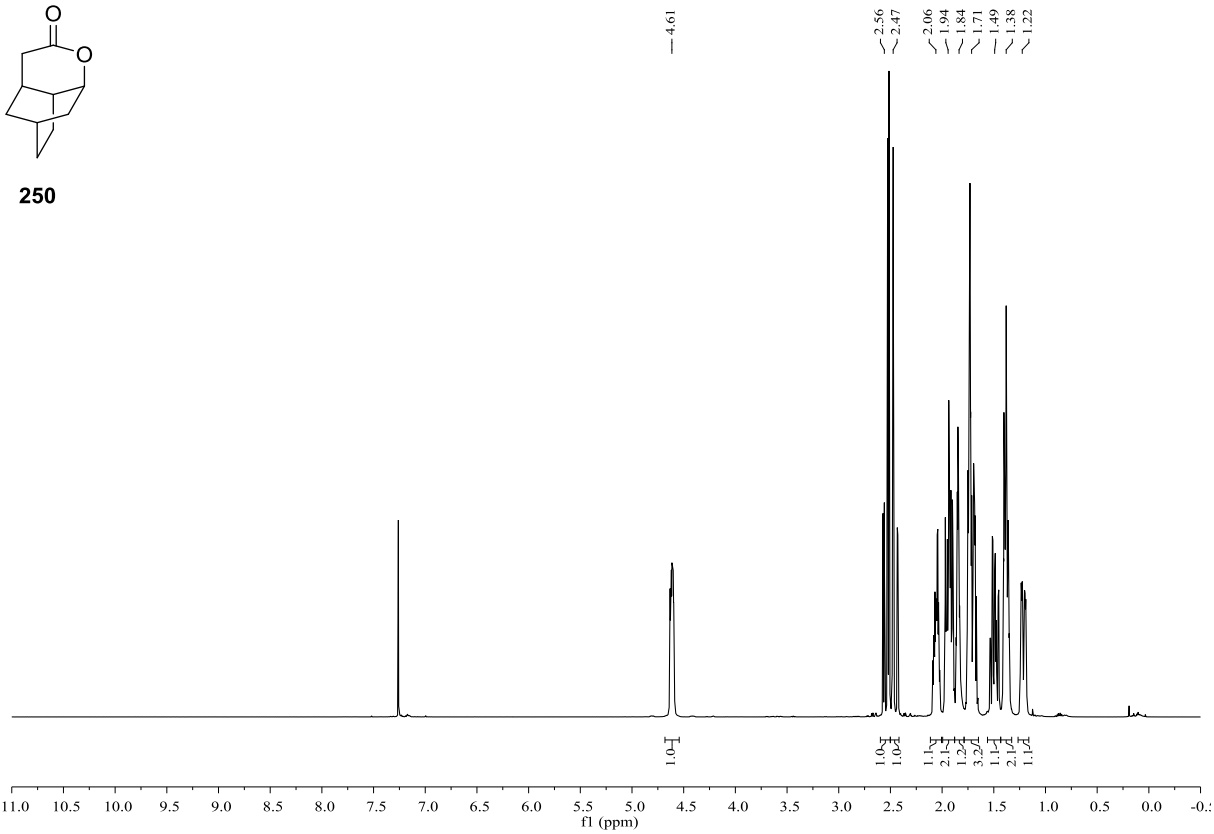


544

544 (^{13}C NMR, 150 MHz, $CDCl_3$)

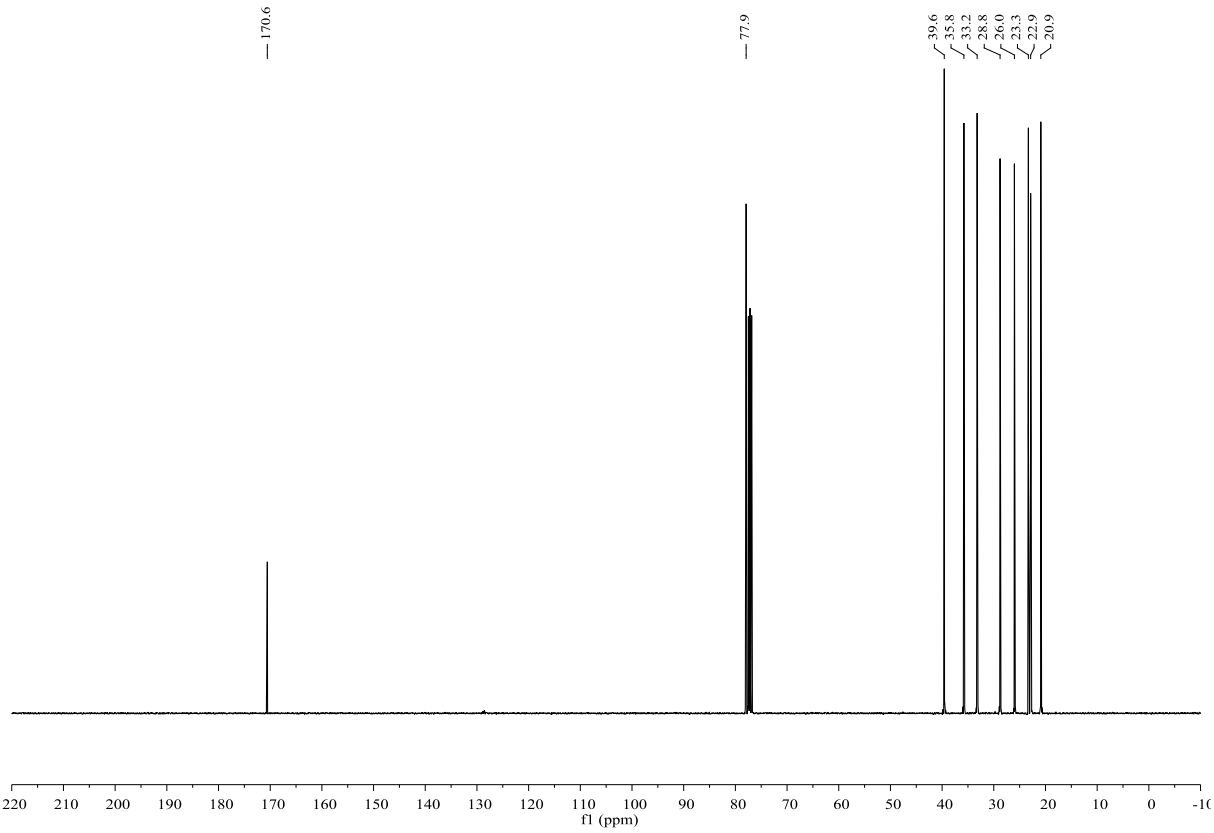


250 (^{1}H NMR, 400 MHz, $CDCl_3$)

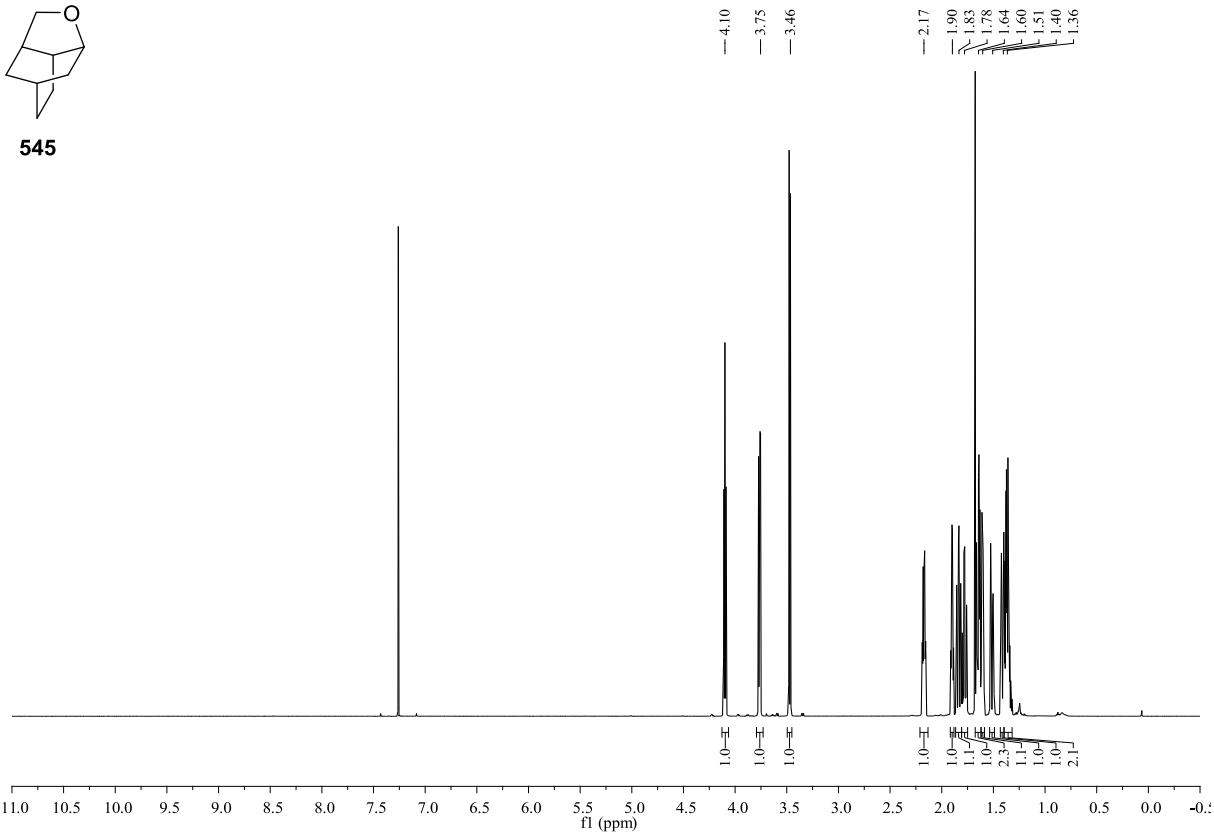


250

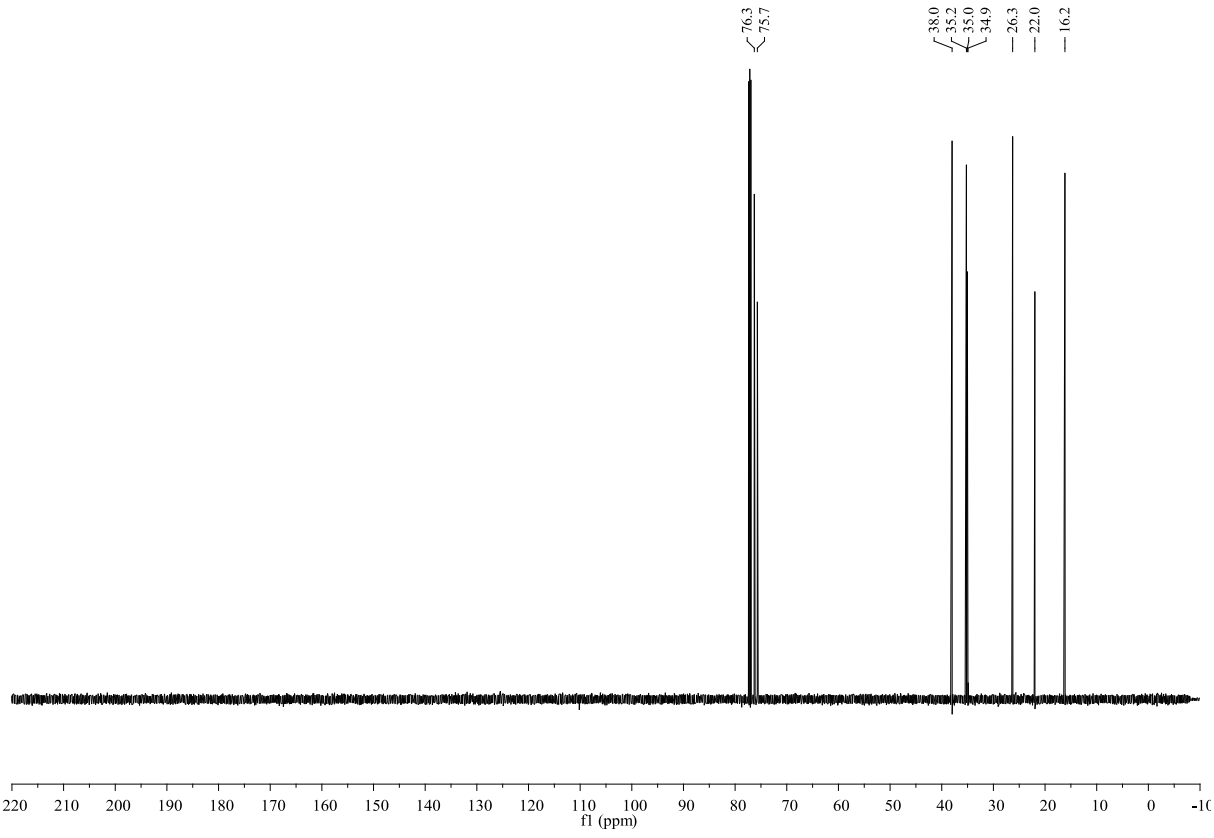
250 (^{13}C NMR, 100 MHz, $CDCl_3$)



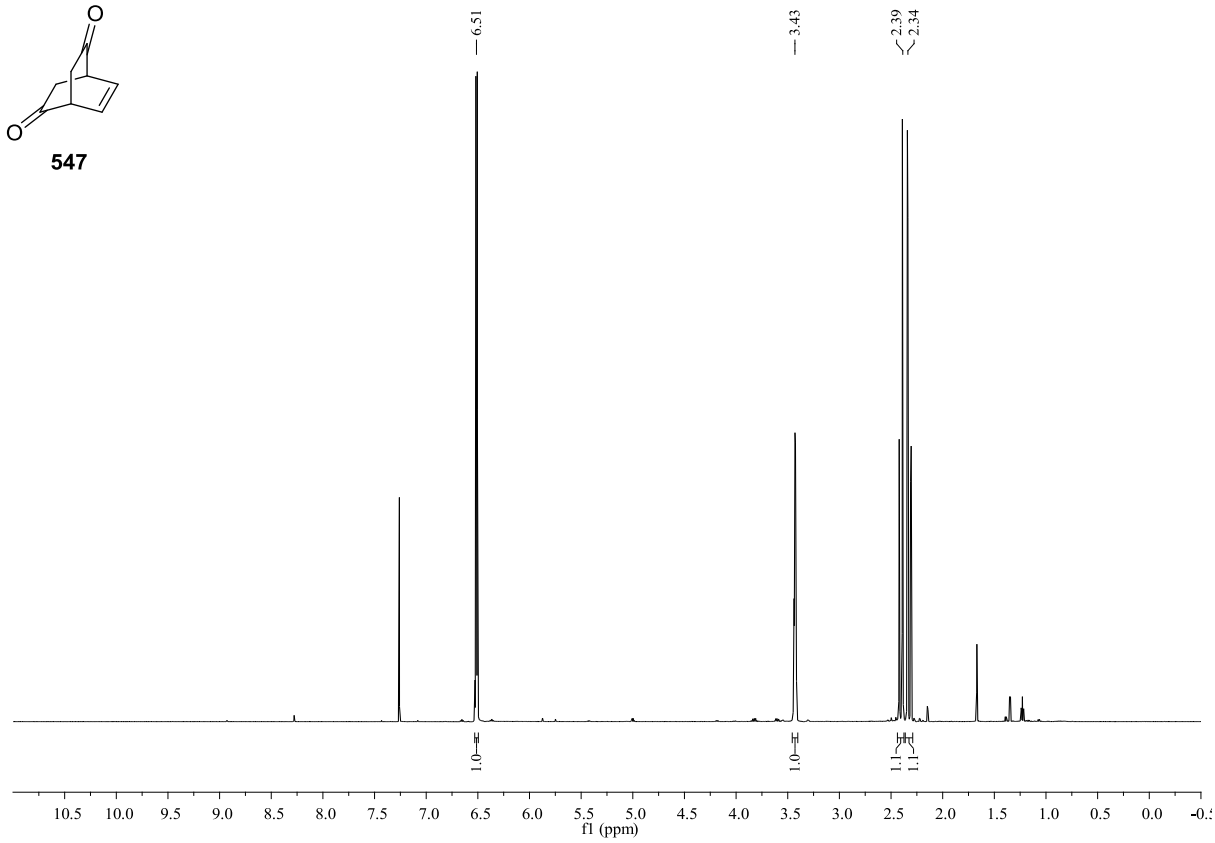
545 (^{1}H NMR, 600 MHz, $CDCl_3$)



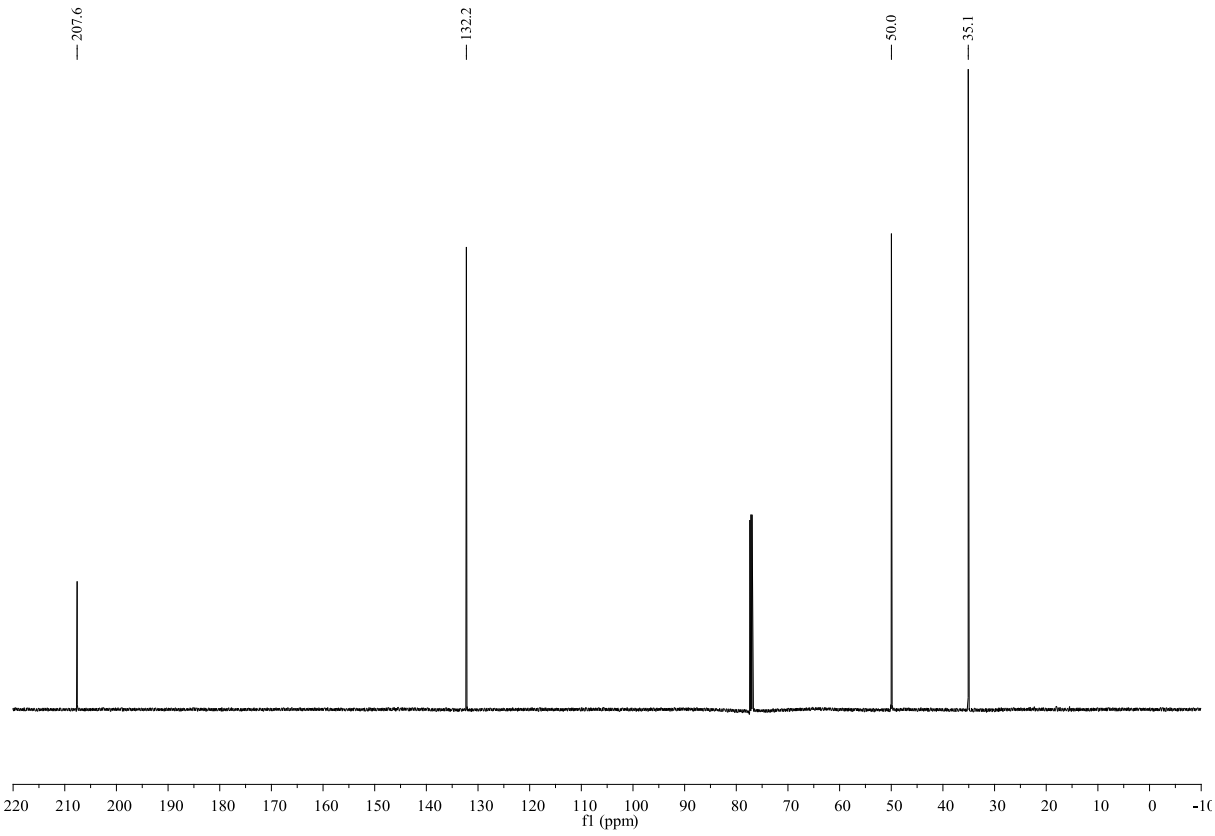
545 (^{13}C NMR, 150 MHz, $CDCl_3$)



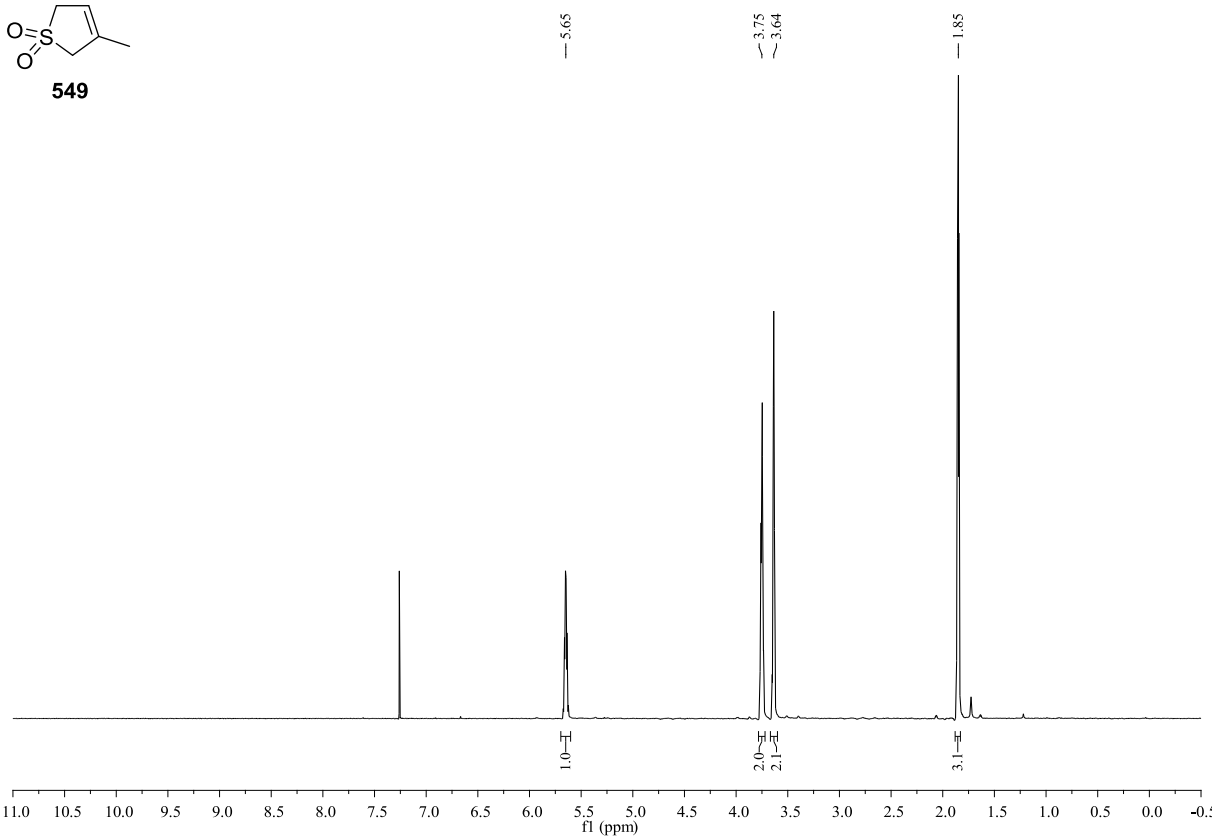
547 (^{1}H NMR, 600 MHz, $CDCl_3$)



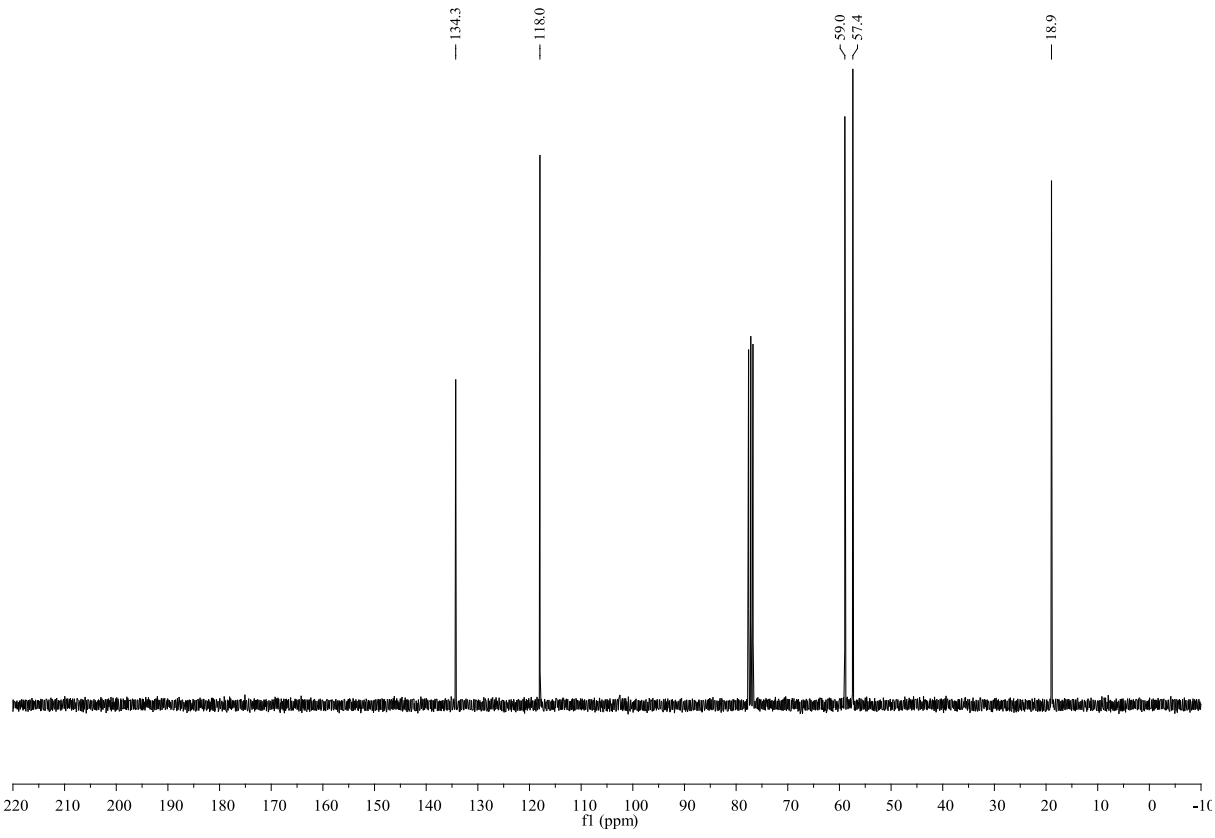
547 (^{13}C NMR, 150 MHz, $CDCl_3$)



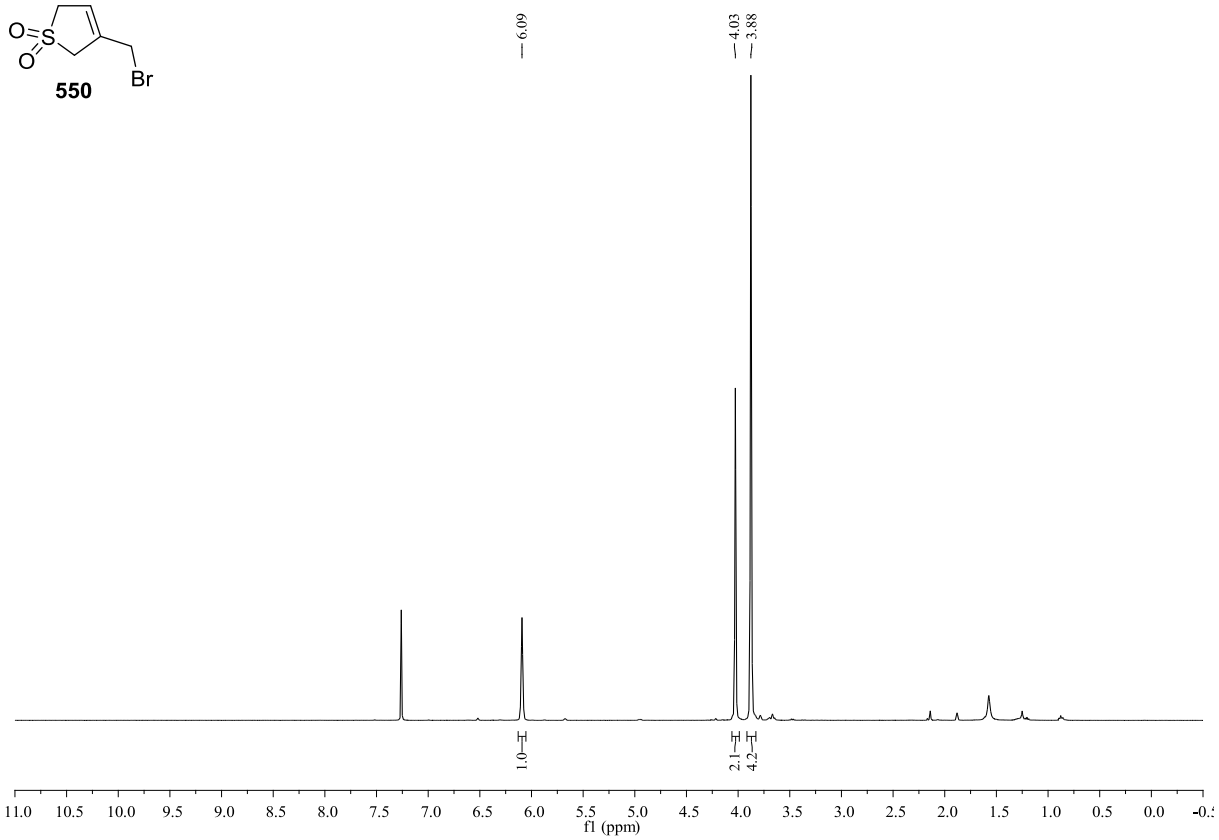
549 (^{1}H NMR, 300 MHz, $CDCl_3$)



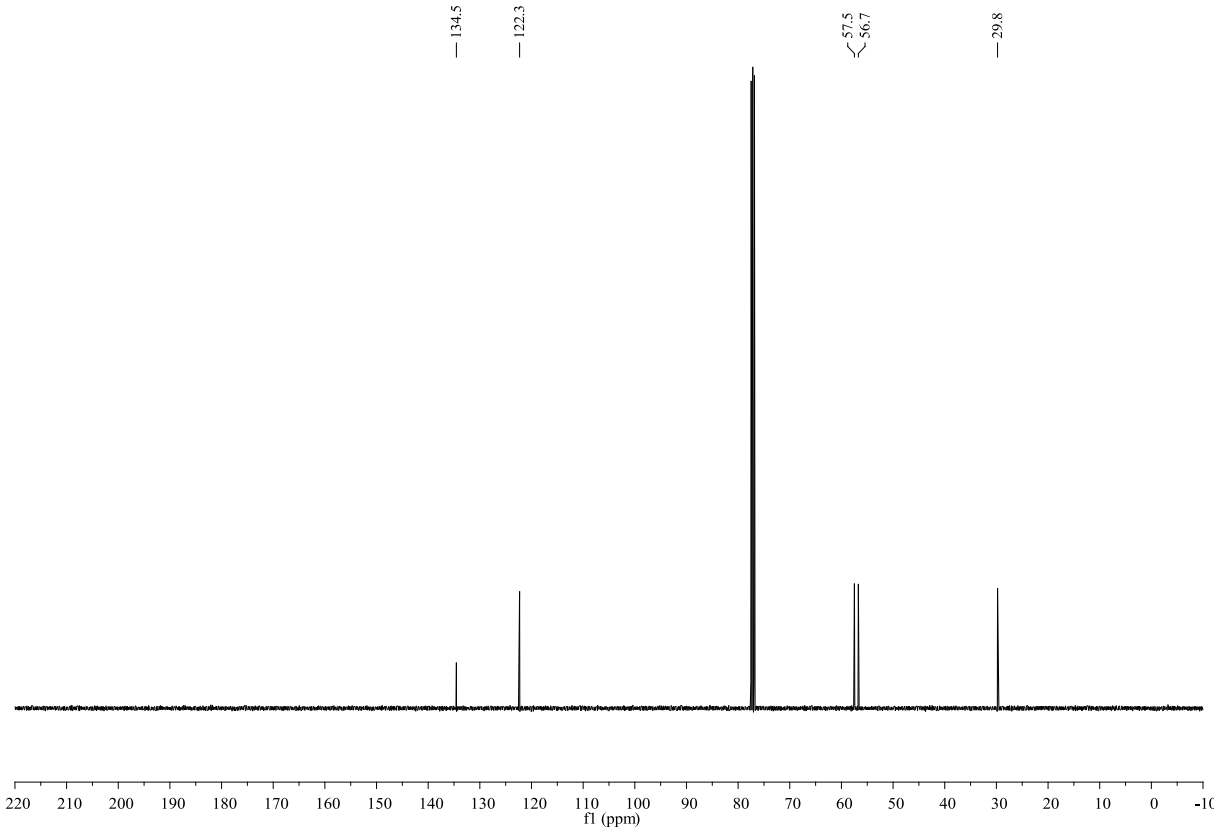
549 (^{13}C NMR, 75 MHz, $CDCl_3$)



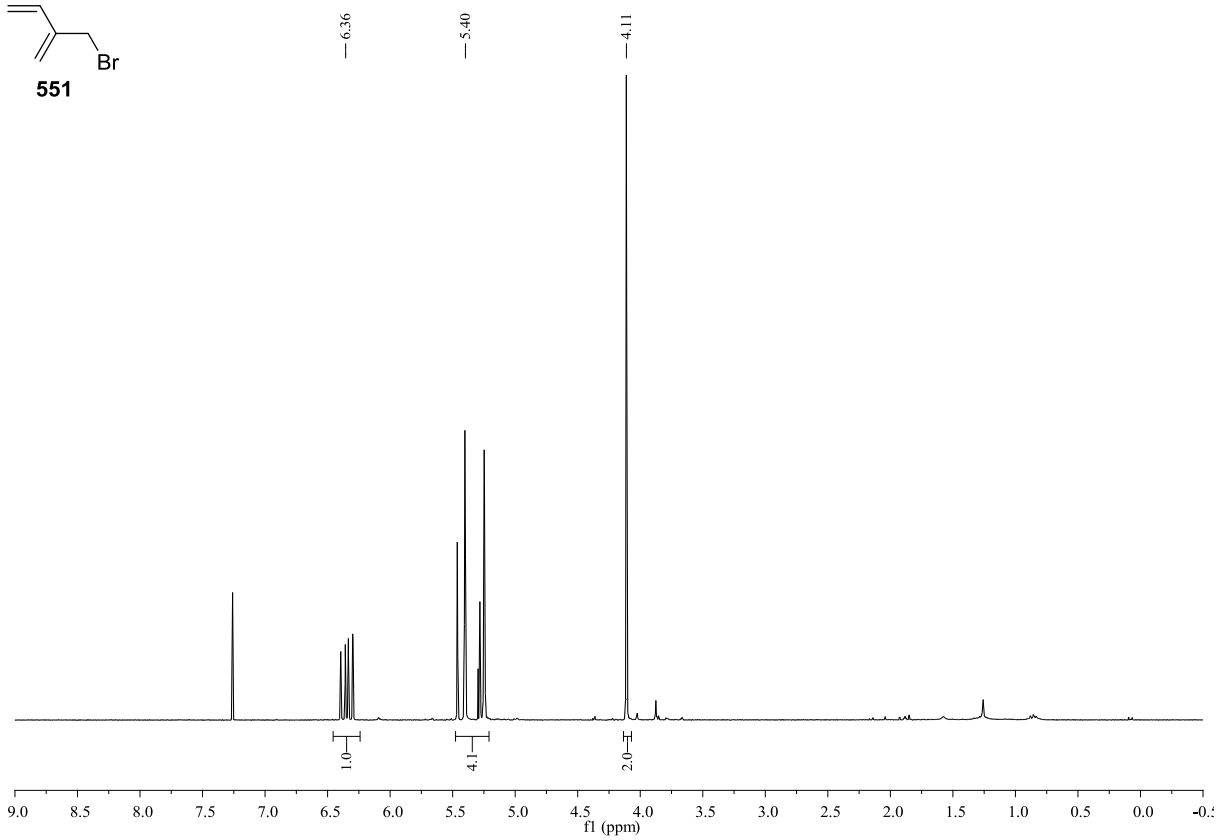
550 (^{1}H NMR, 400 MHz, $CDCl_3$)



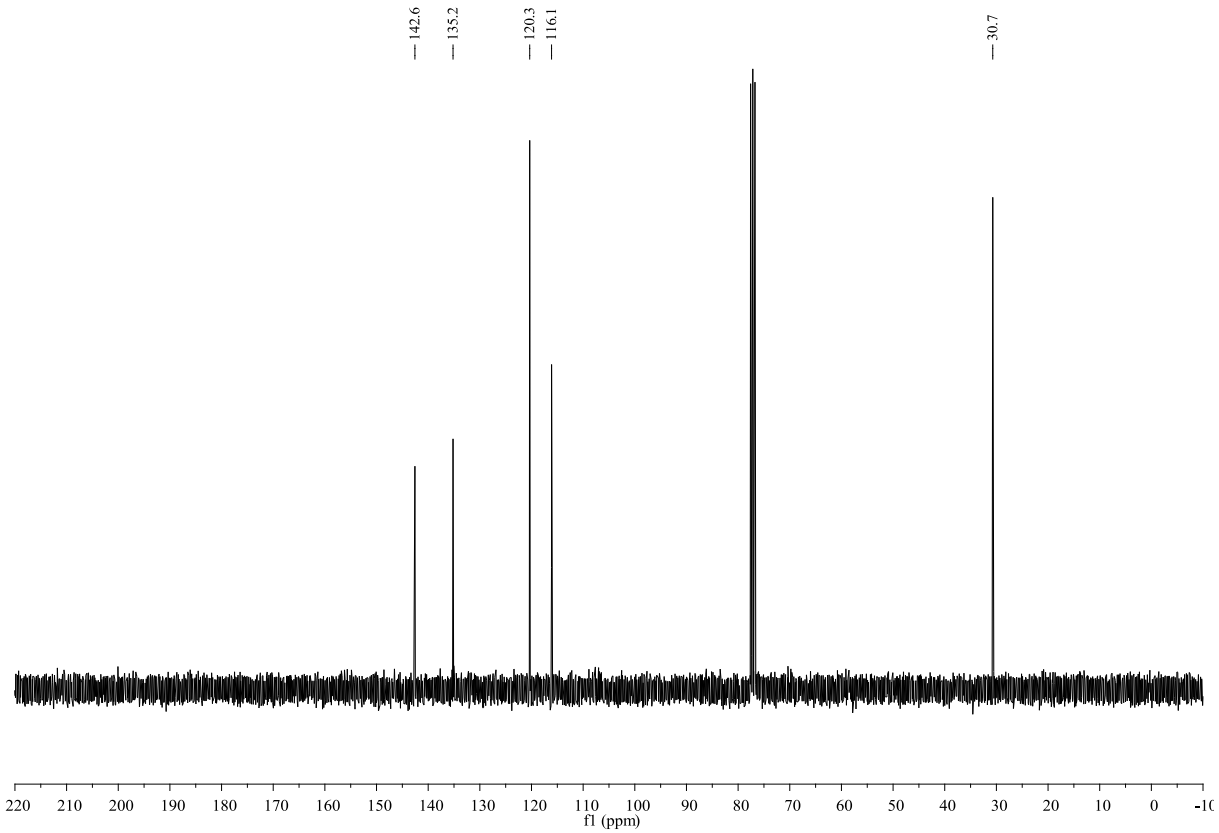
550 (^{13}C NMR, 100 MHz, $CDCl_3$)



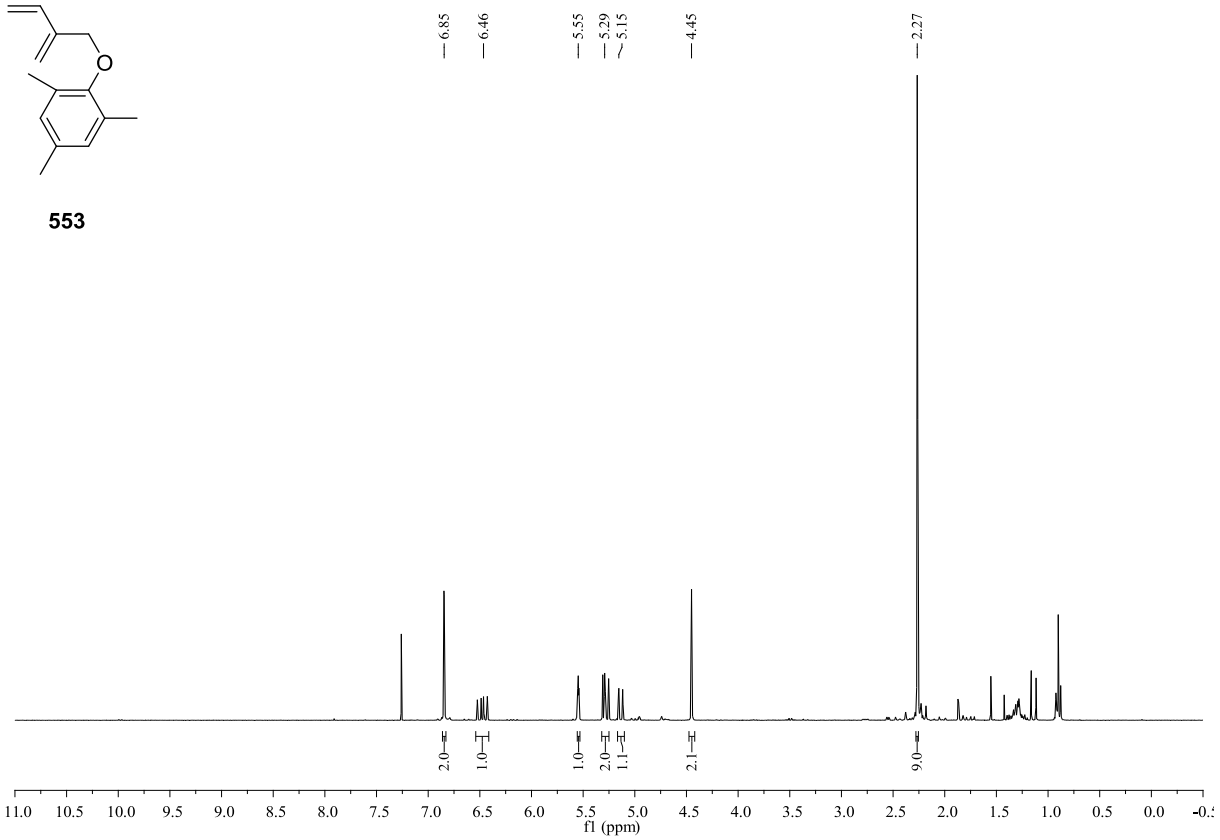
551 (^{1}H NMR, 300 MHz, $CDCl_3$)



551 (^{13}C NMR, 75 MHz, $CDCl_3$)

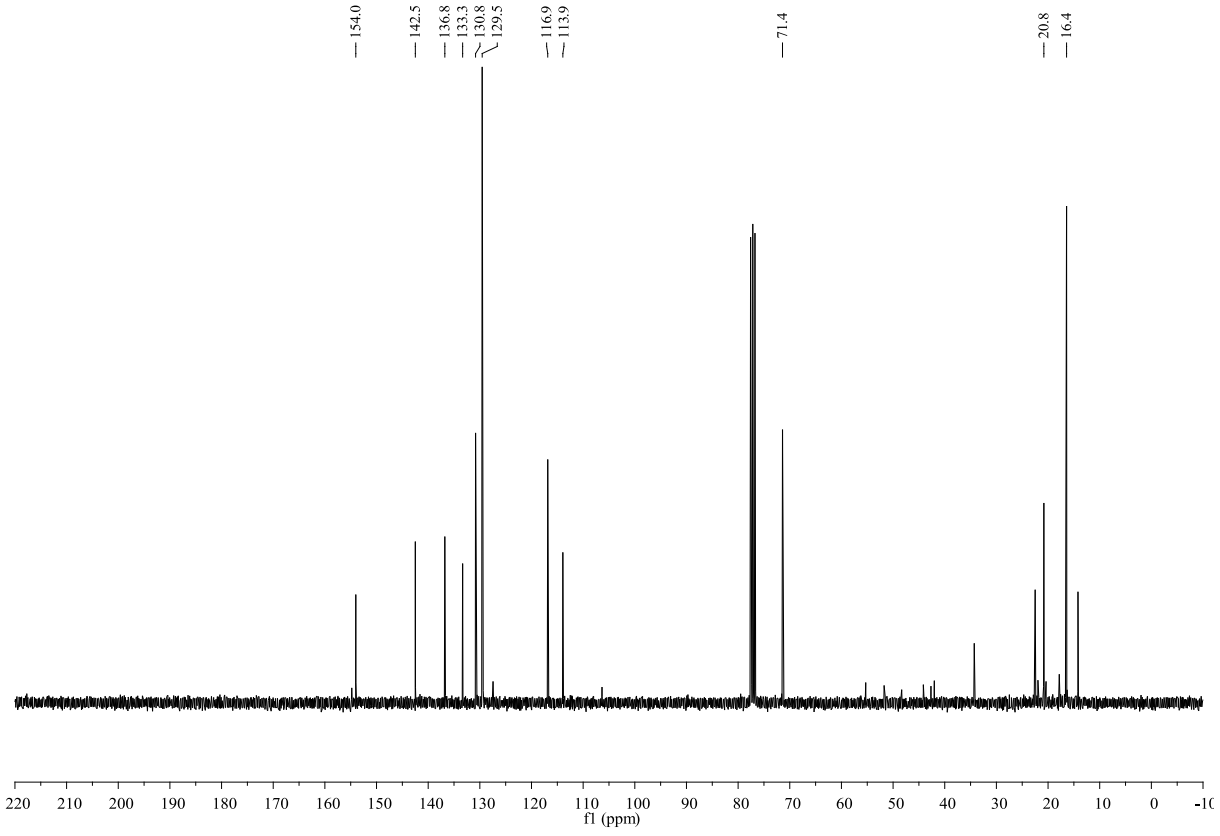


553 (^{1}H NMR, 300 MHz, $CDCl_3$)

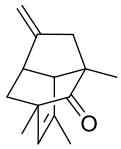


553

553 (^{13}C NMR, 75 MHz, $CDCl_3$)

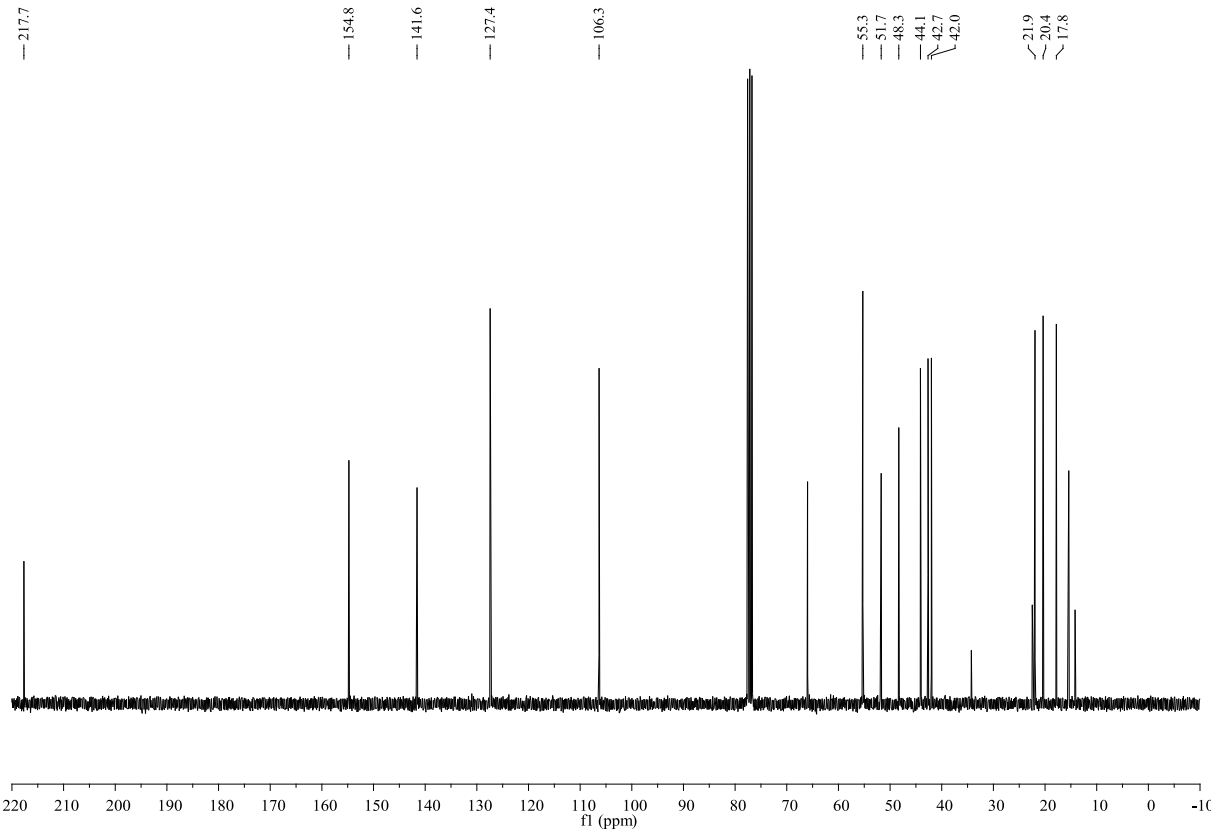


556 (^{1}H NMR, 300 MHz, $CDCl_3$)

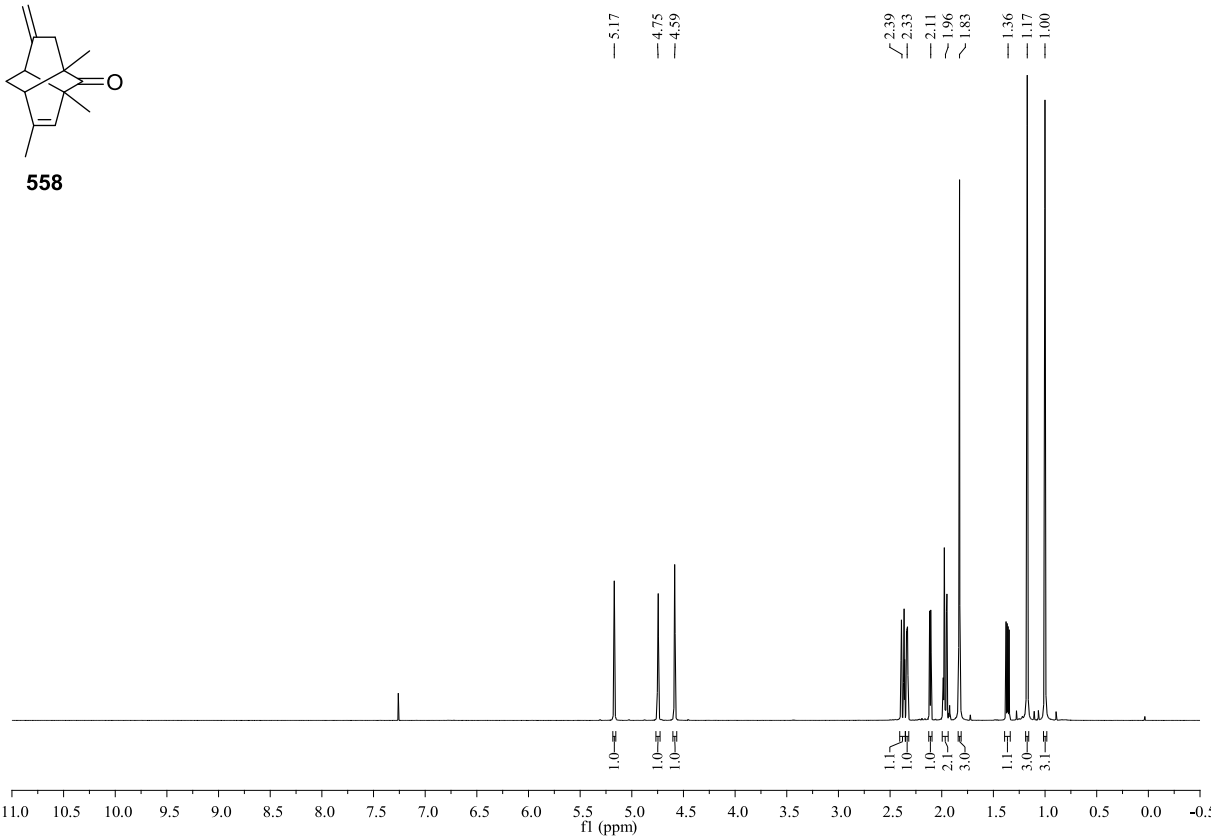


556

556 (^{13}C NMR, 75 MHz, $CDCl_3$)

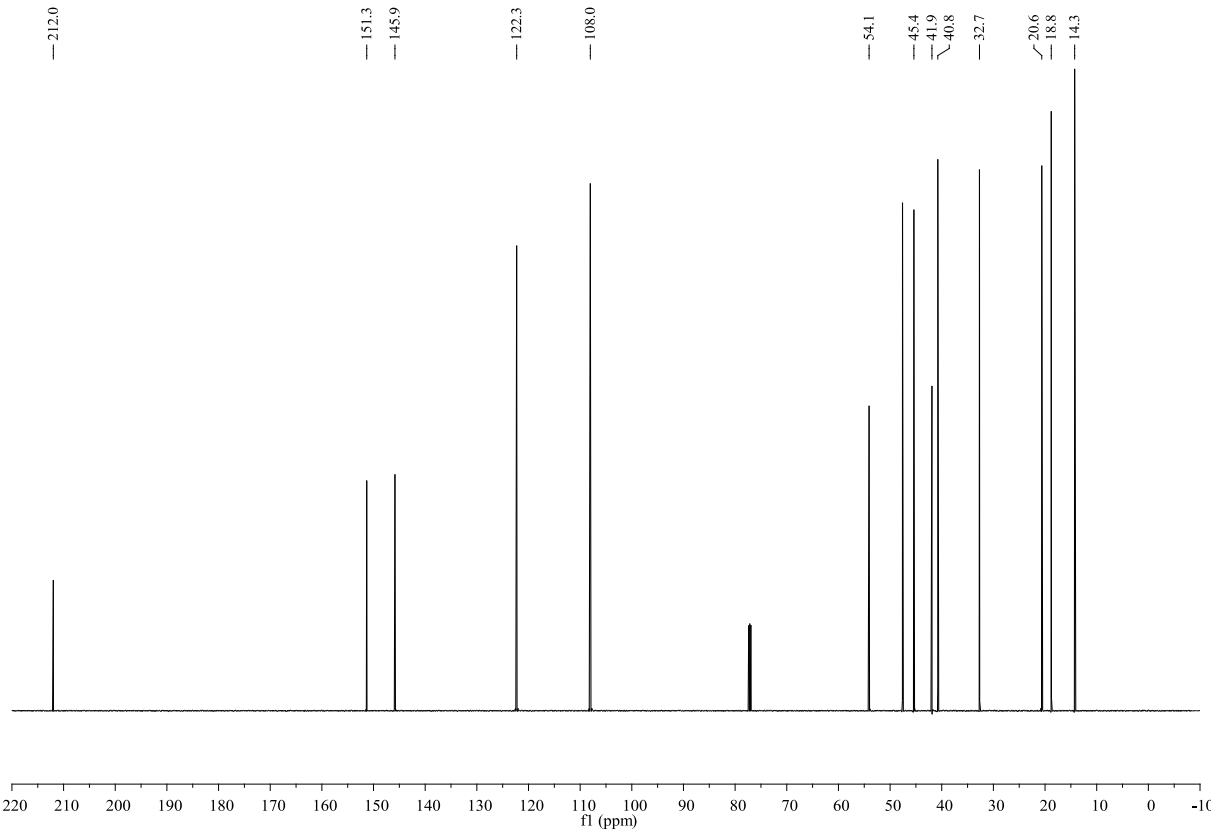


558 (^{1}H NMR, 600 MHz, $CDCl_3$)

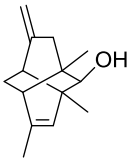


558

558 (^{13}C NMR, 150 MHz, $CDCl_3$)

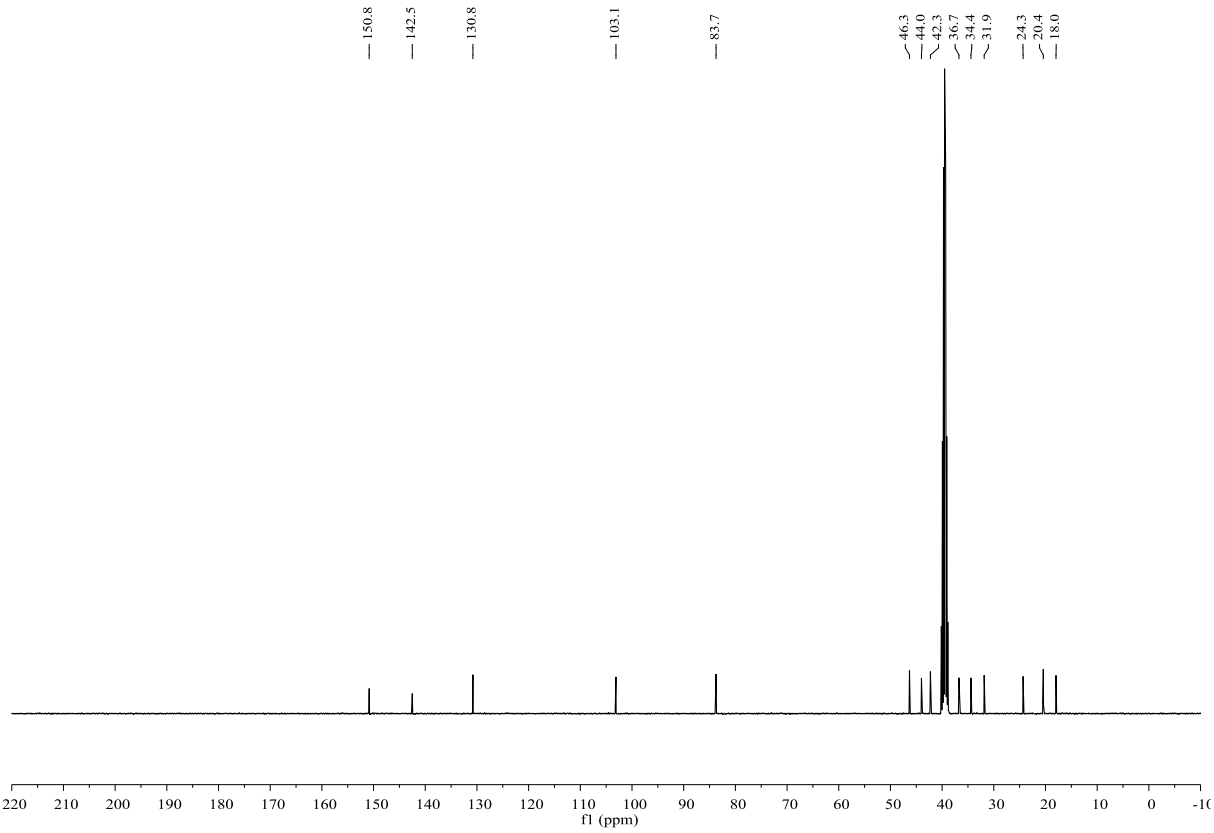


***exo*-559** (^{1}H NMR, 400 MHz, DMSO-d_6)

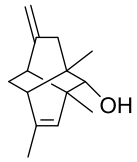


***exo*-559**

***exo*-559** (^{13}C NMR, 100 MHz, DMSO-d_6)

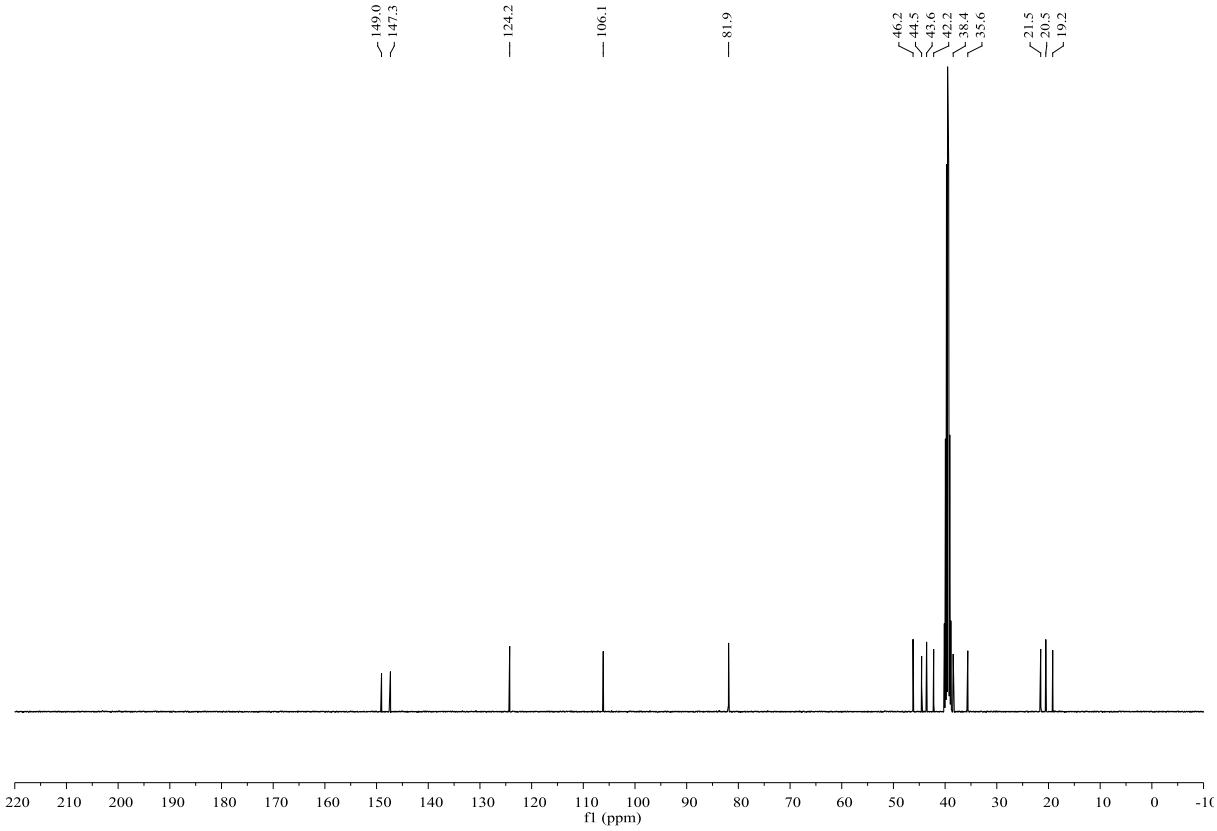


***endo*-559** (^{1}H NMR, 400 MHz, DMSO-d_6)

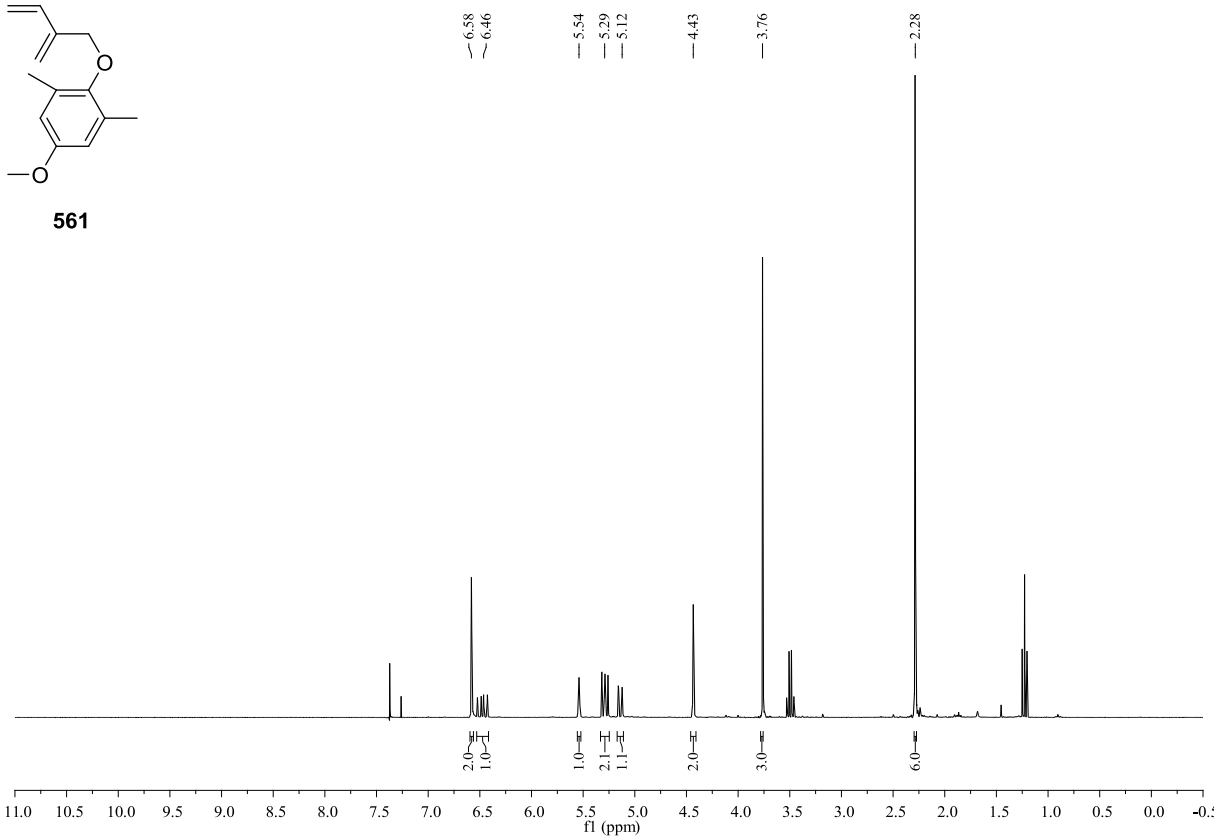


***endo*-559**

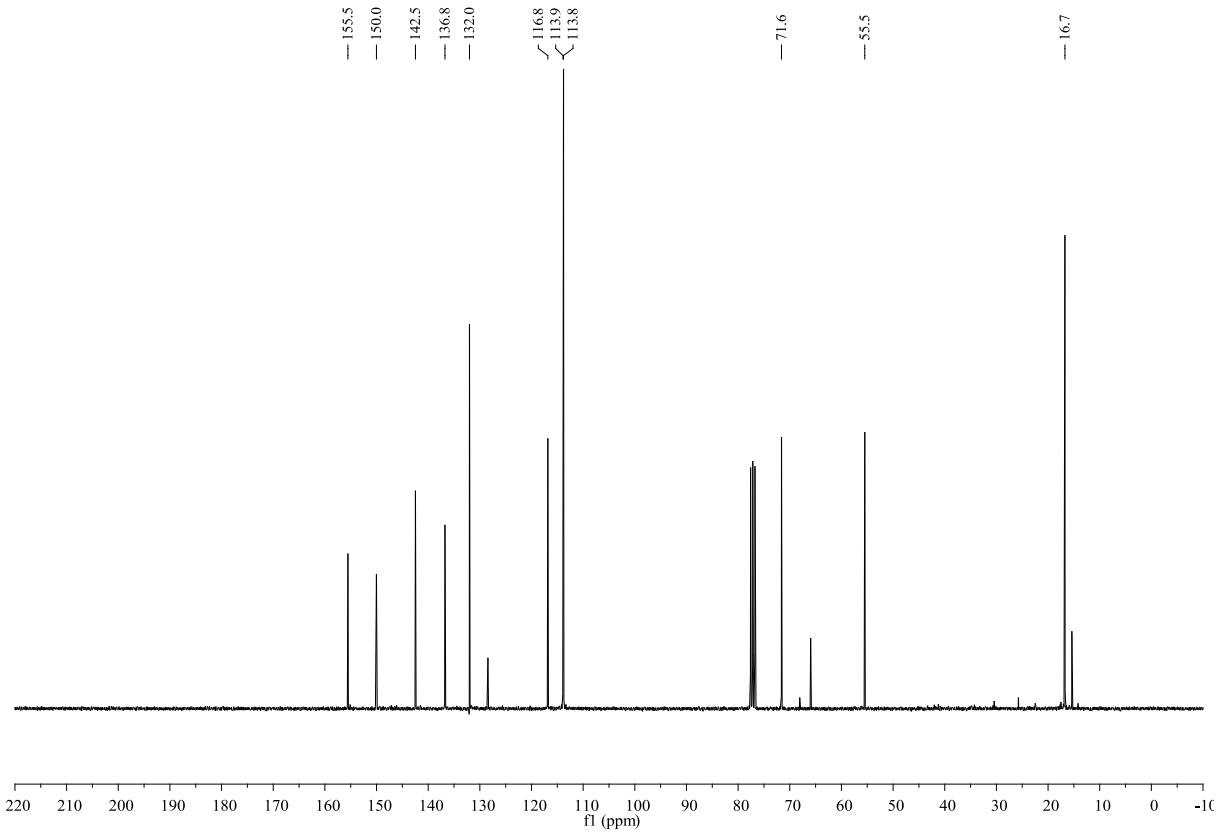
***endo*-559** (^{13}C NMR, 100 MHz, DMSO-d_6)



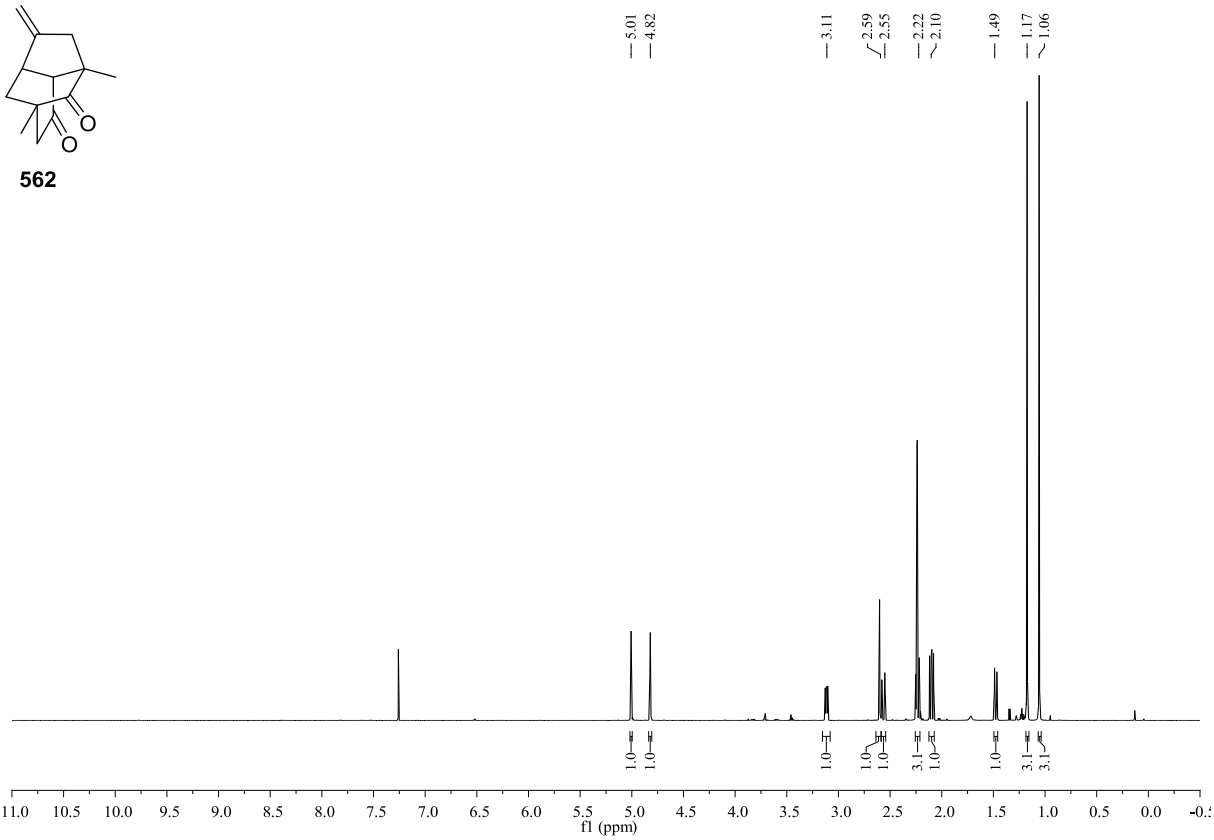
561 (^{1}H NMR, 300 MHz, $CDCl_3$)



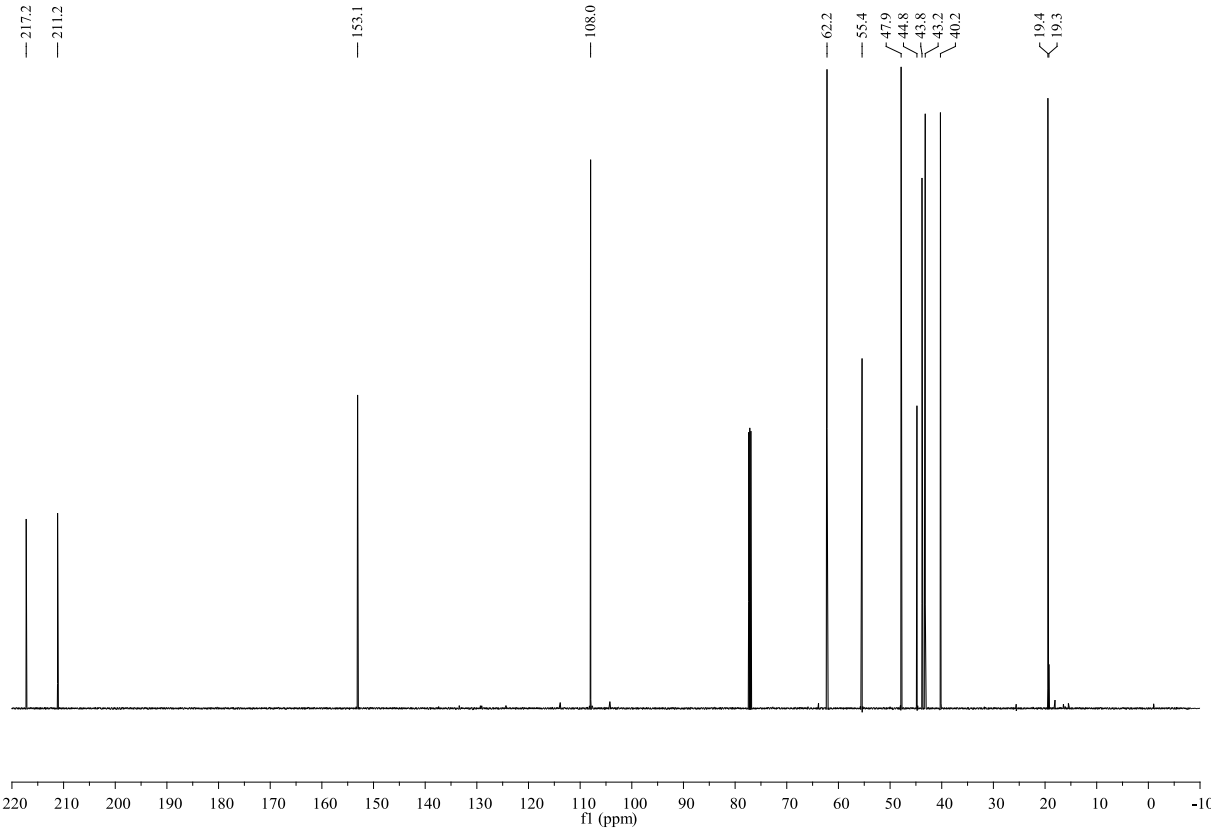
561 (^{13}C NMR, 75 MHz, $CDCl_3$)



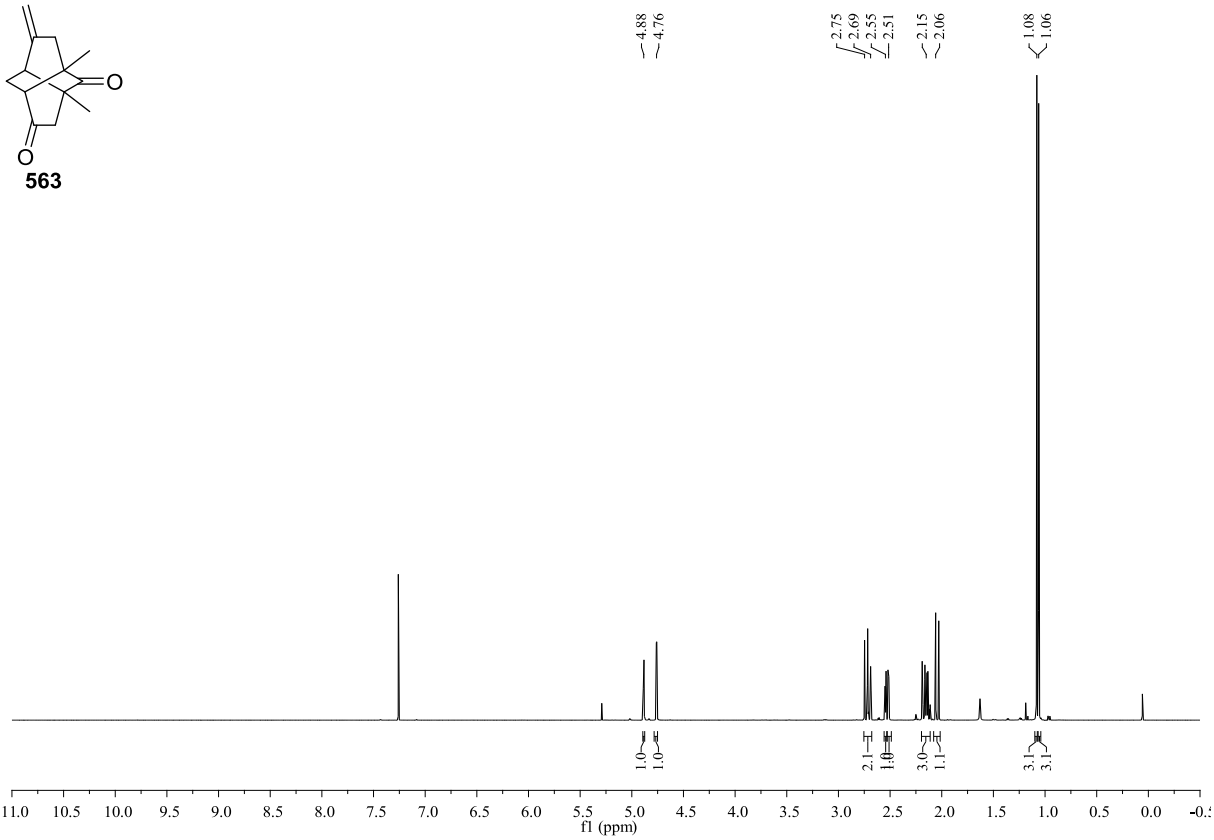
562 (^{1}H NMR, 600 MHz, $CDCl_3$)



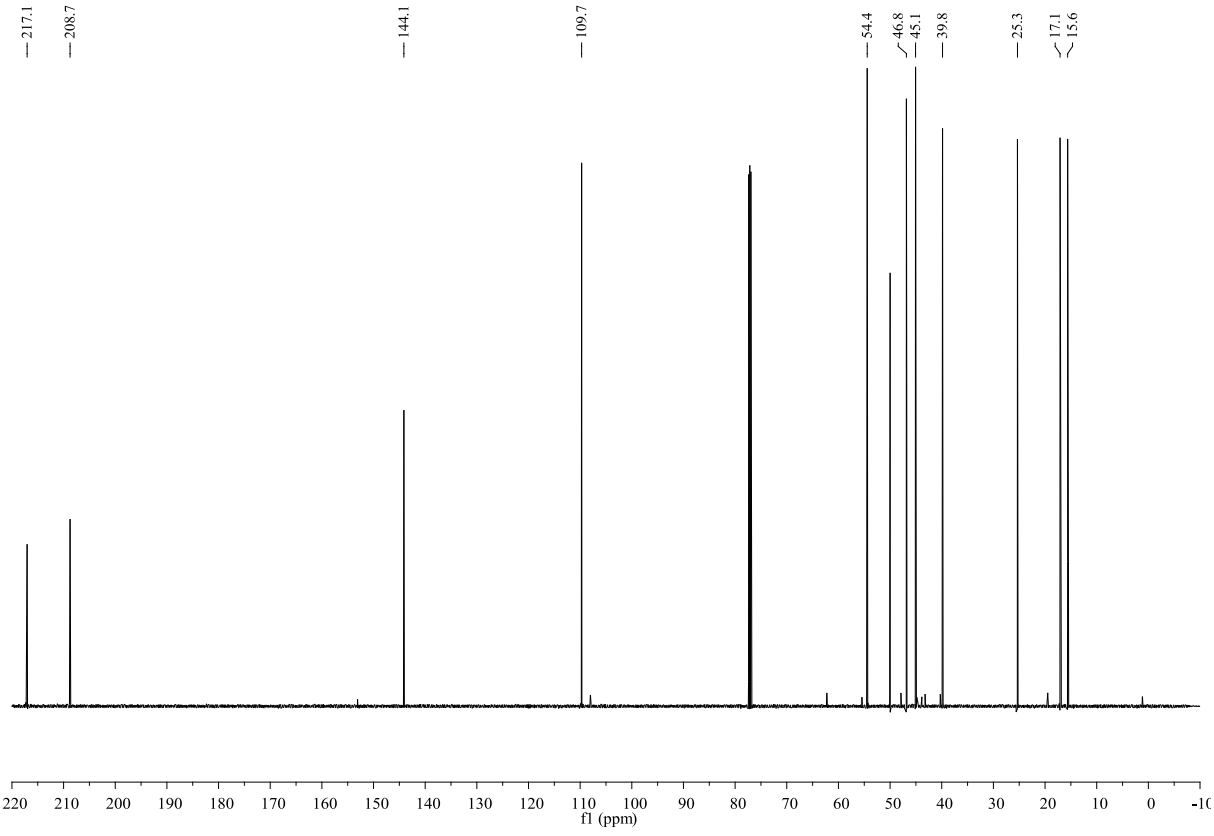
562 (^{13}C NMR, 150 MHz, $CDCl_3$)



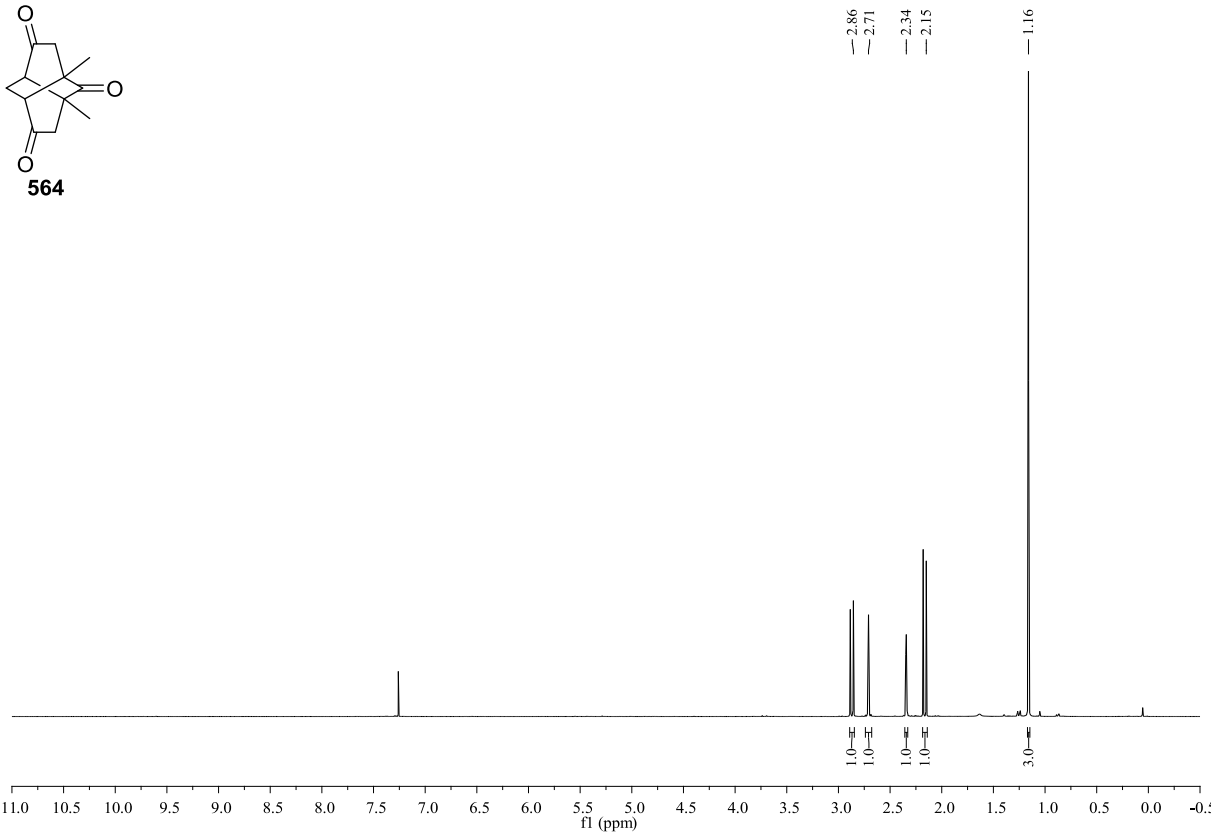
563 (^{1}H NMR, 600 MHz, $CDCl_3$)



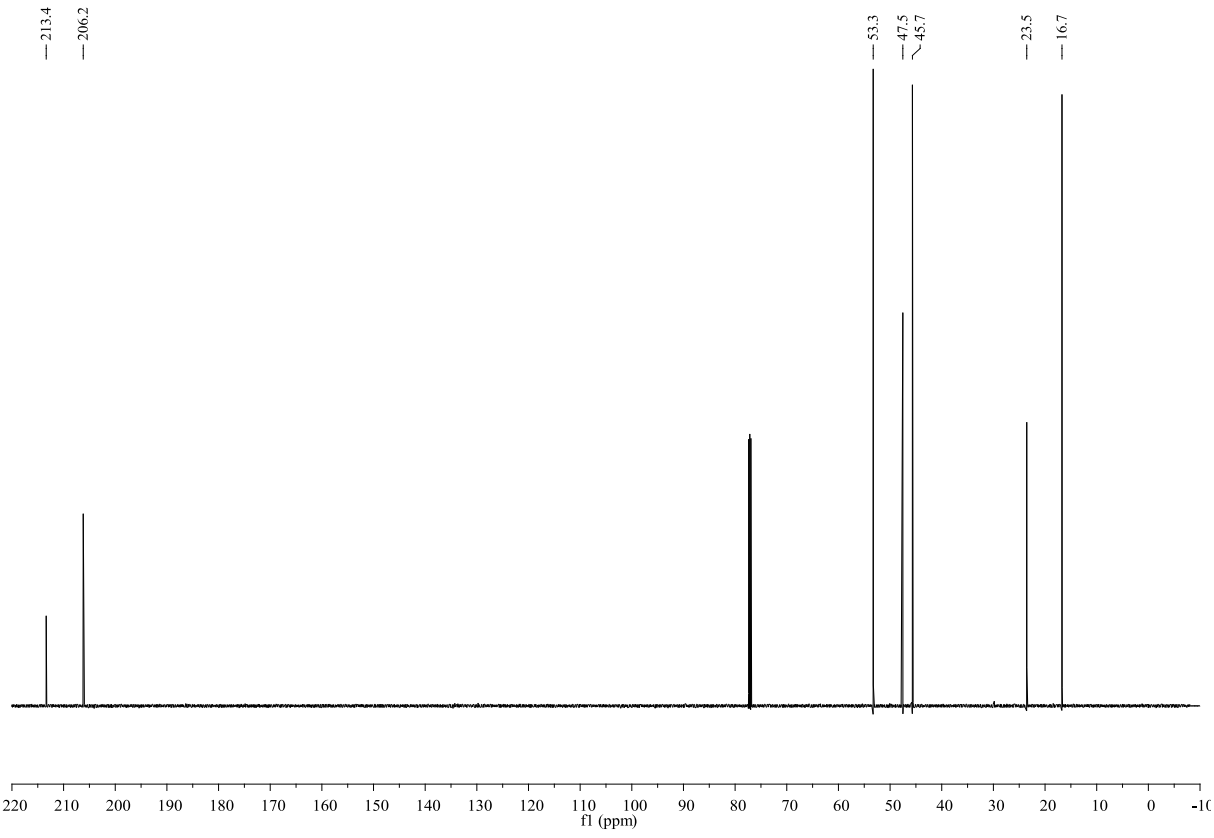
563 (^{13}C NMR, 150 MHz, $CDCl_3$)



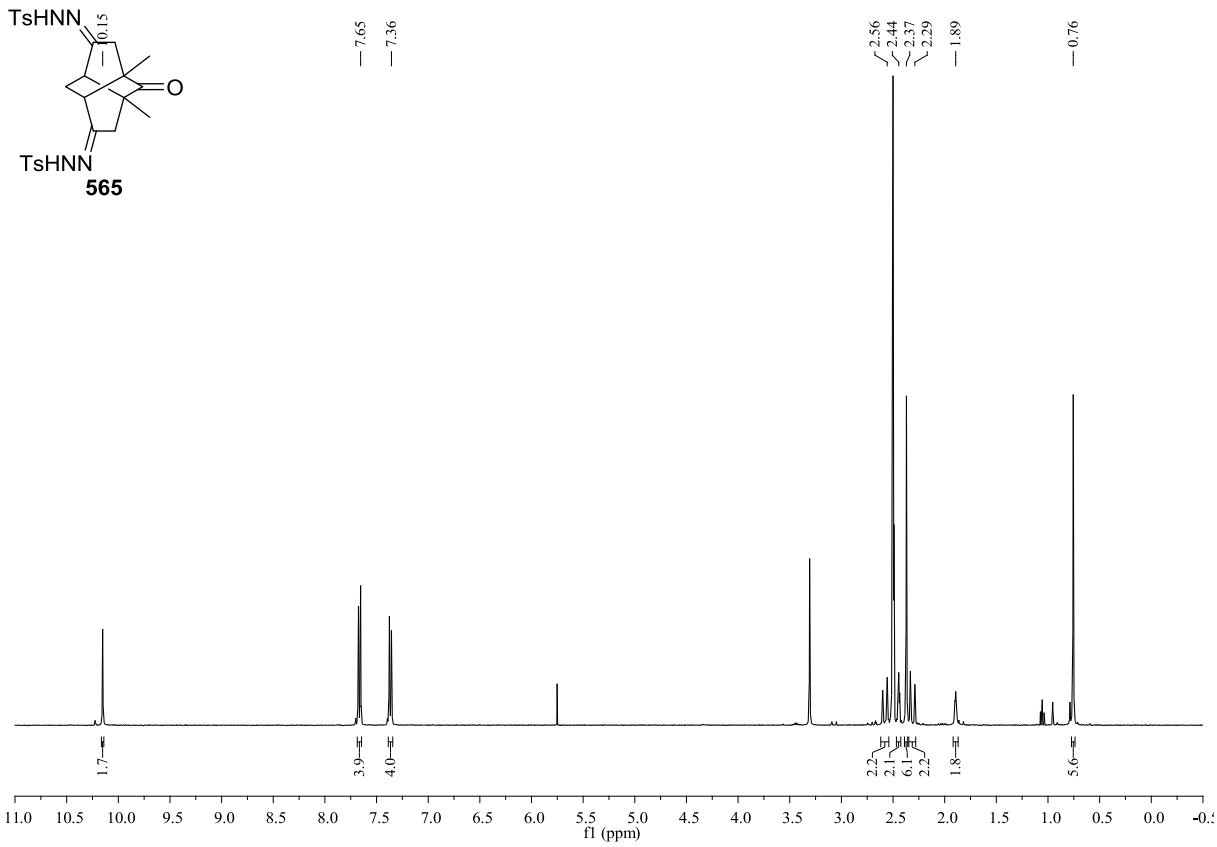
564 (^{1}H NMR, 600 MHz, $CDCl_3$)



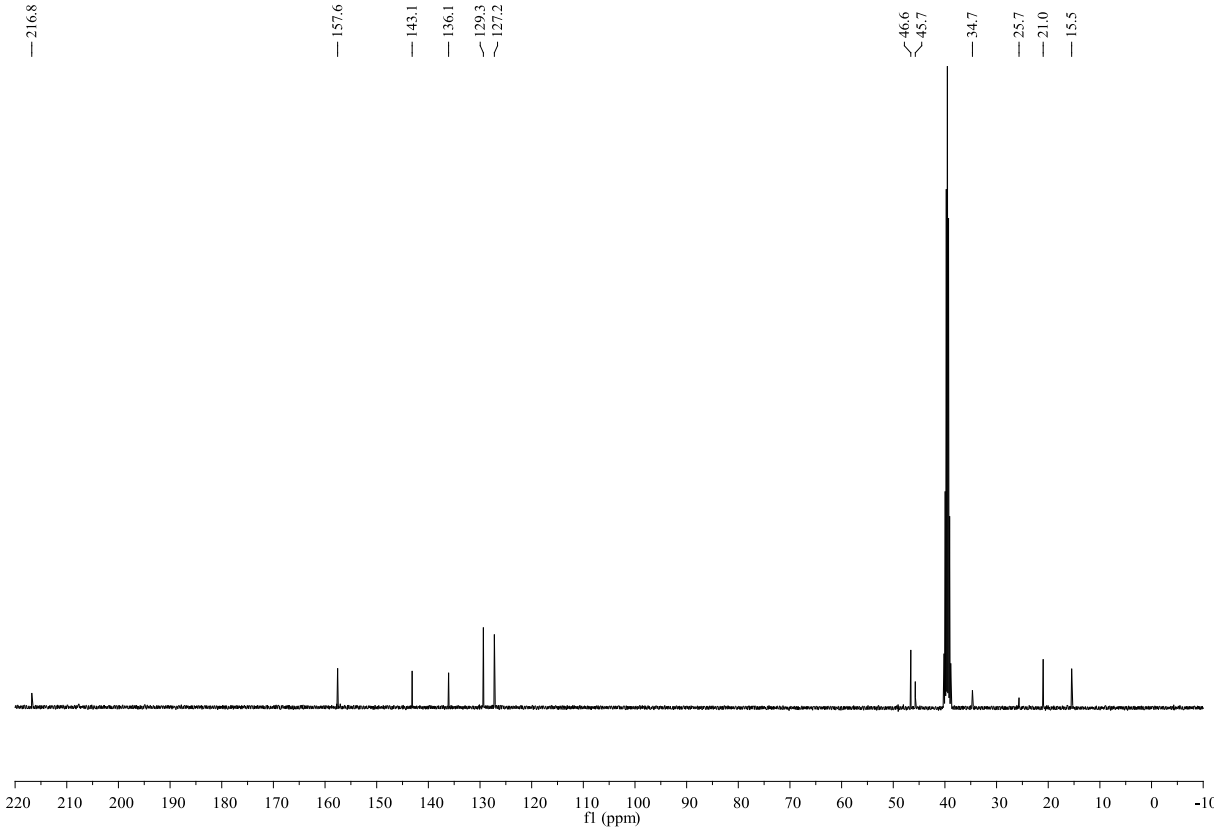
564 (^{13}C NMR, 150 MHz, $CDCl_3$)



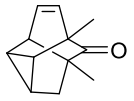
565 (^{1}H NMR, 400 MHz, DMSO-d_6)



565 (^{13}C NMR, 100 MHz, DMSO-d_6)

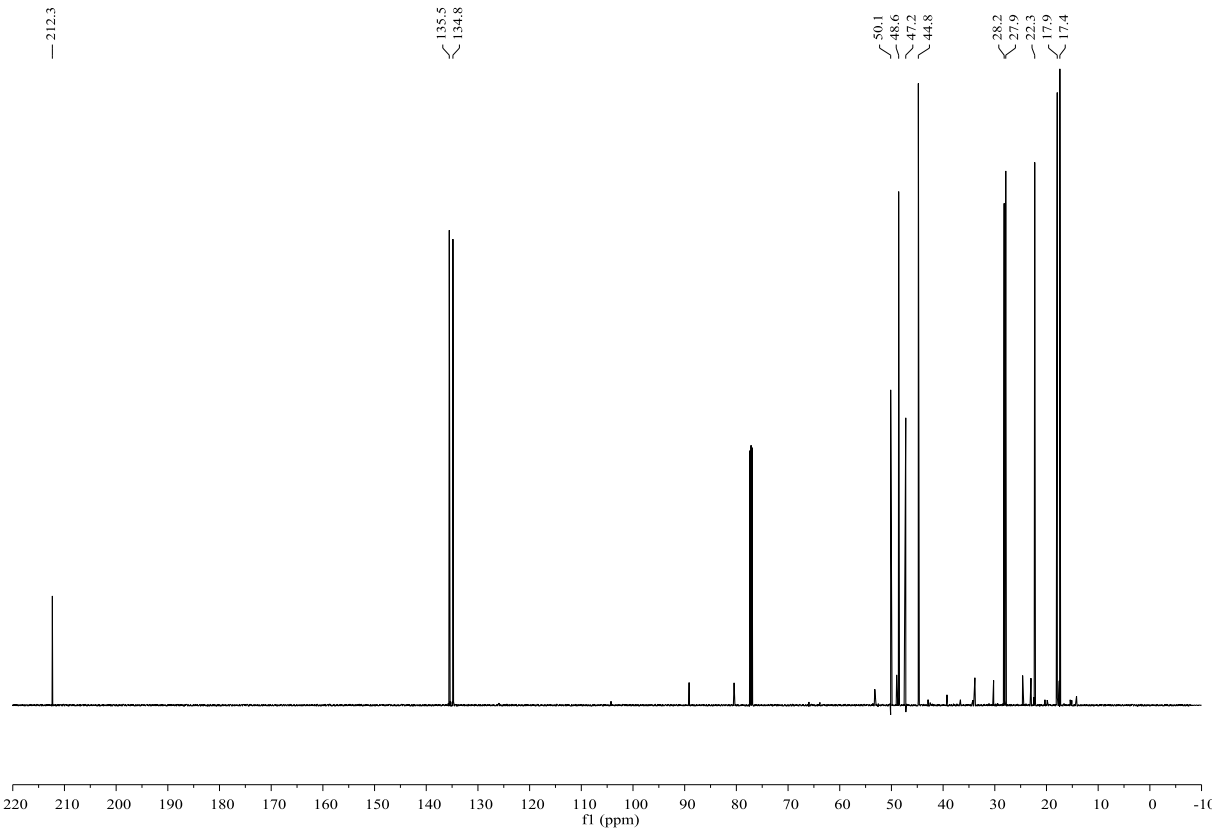


567 (^{1}H NMR, 400 MHz, $CDCl_3$)

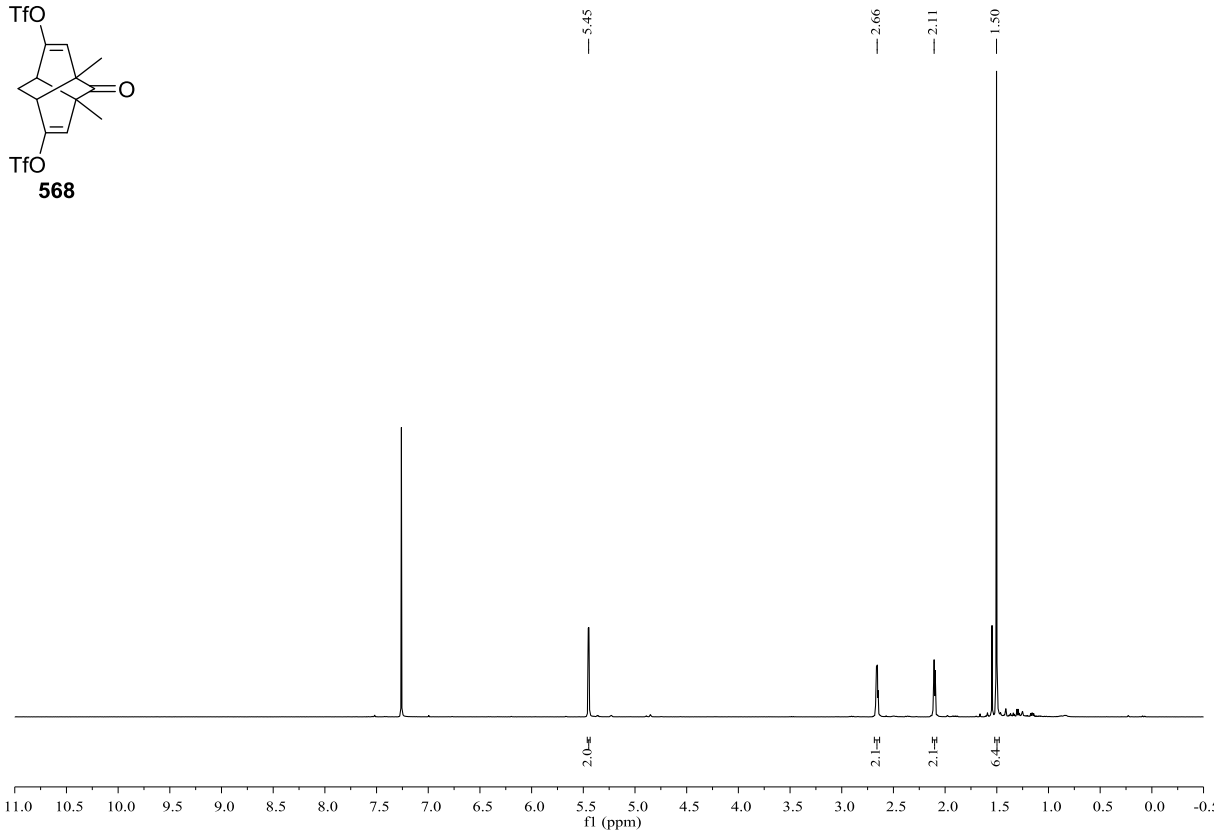


567

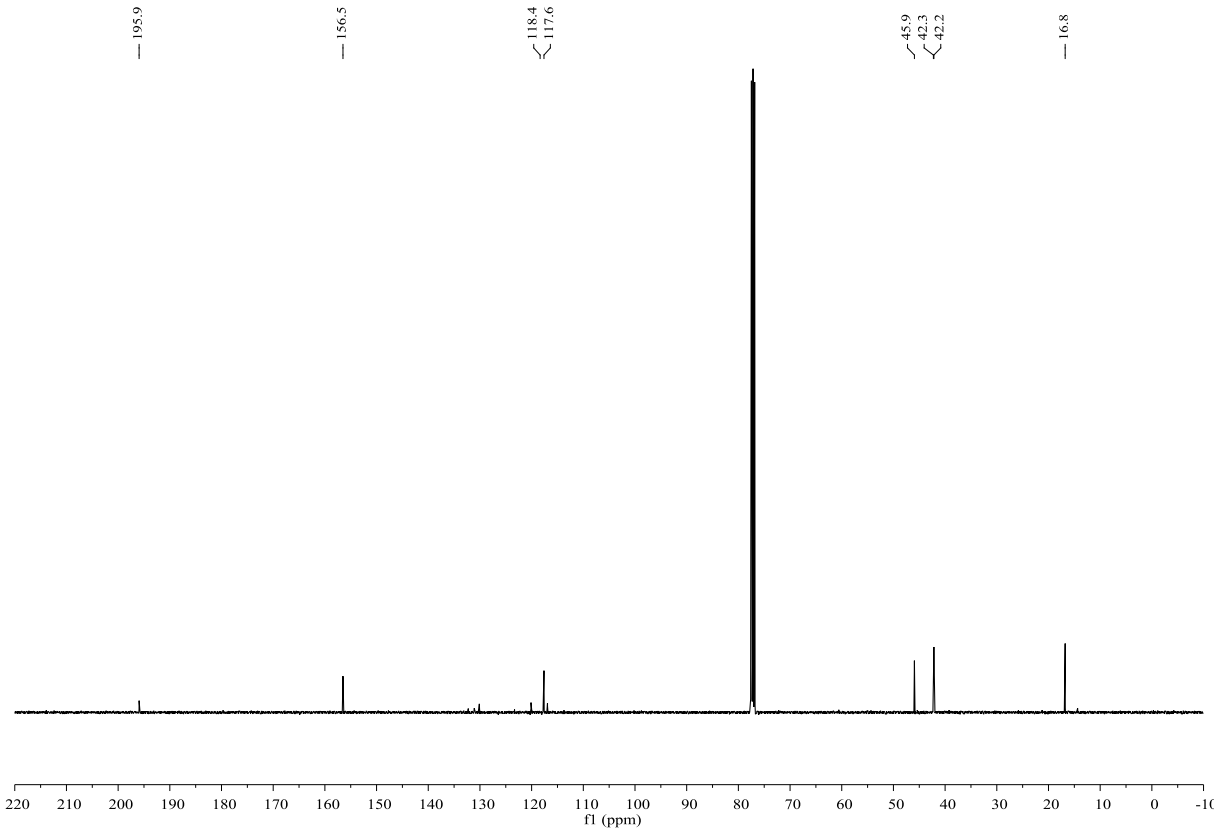
567 (^{13}C NMR, 150 MHz, $CDCl_3$)



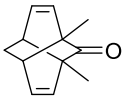
568 (^{1}H NMR, 400 MHz, $CDCl_3$)



568 (^{13}C NMR, 100 MHz, $CDCl_3$)

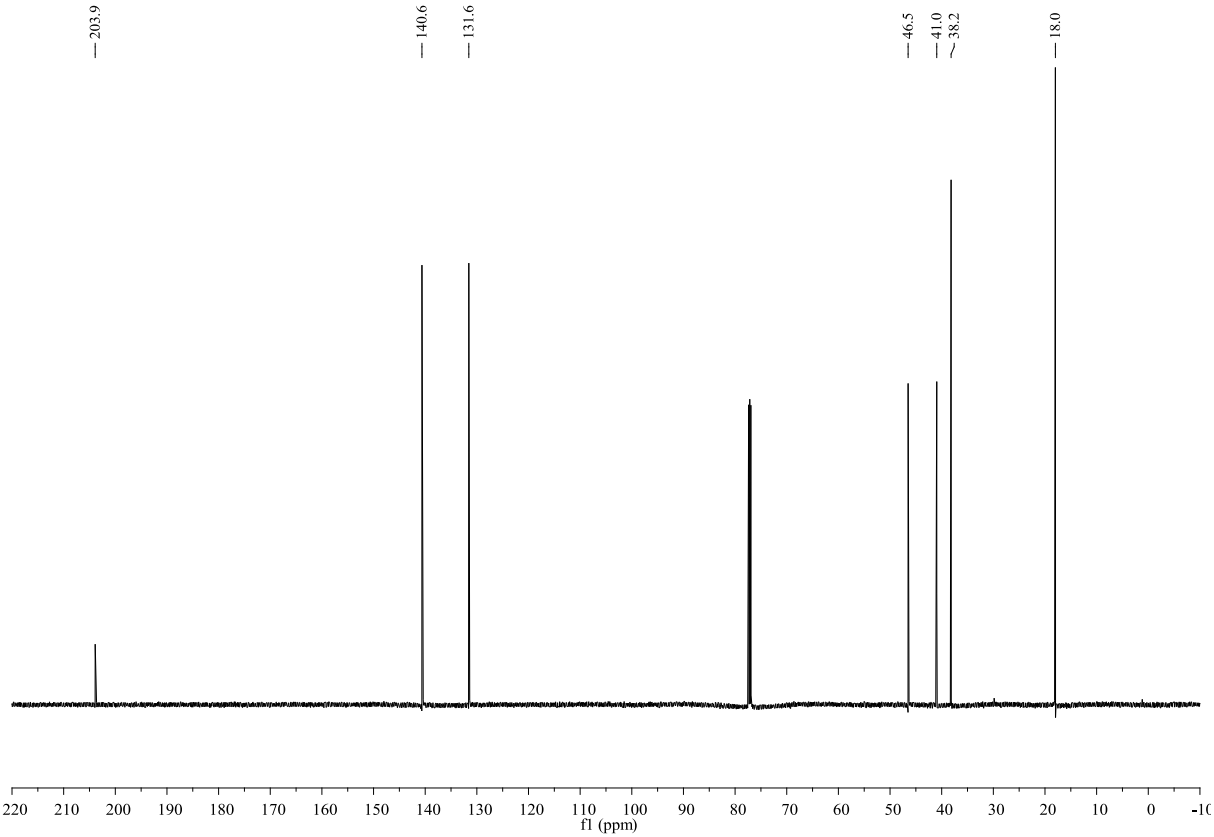


569 (^{1}H NMR, 600 MHz, $CDCl_3$)

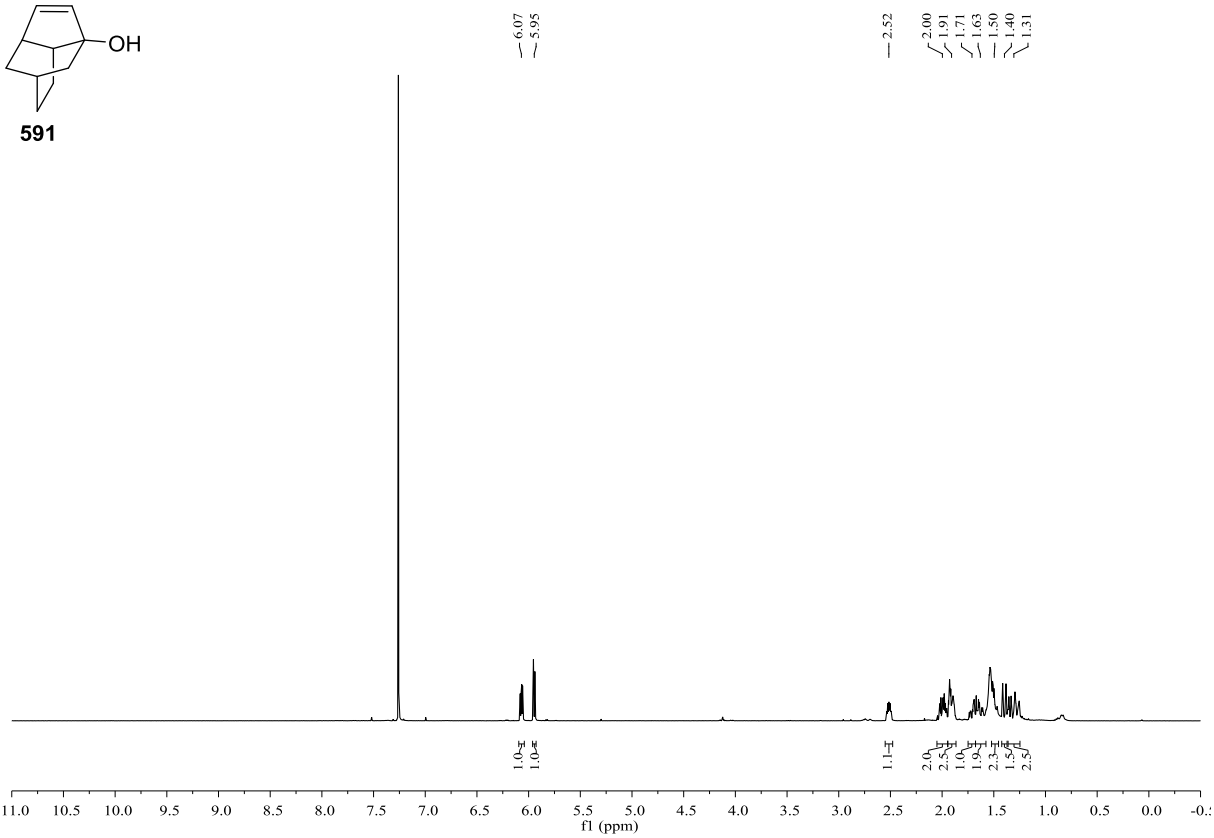


569

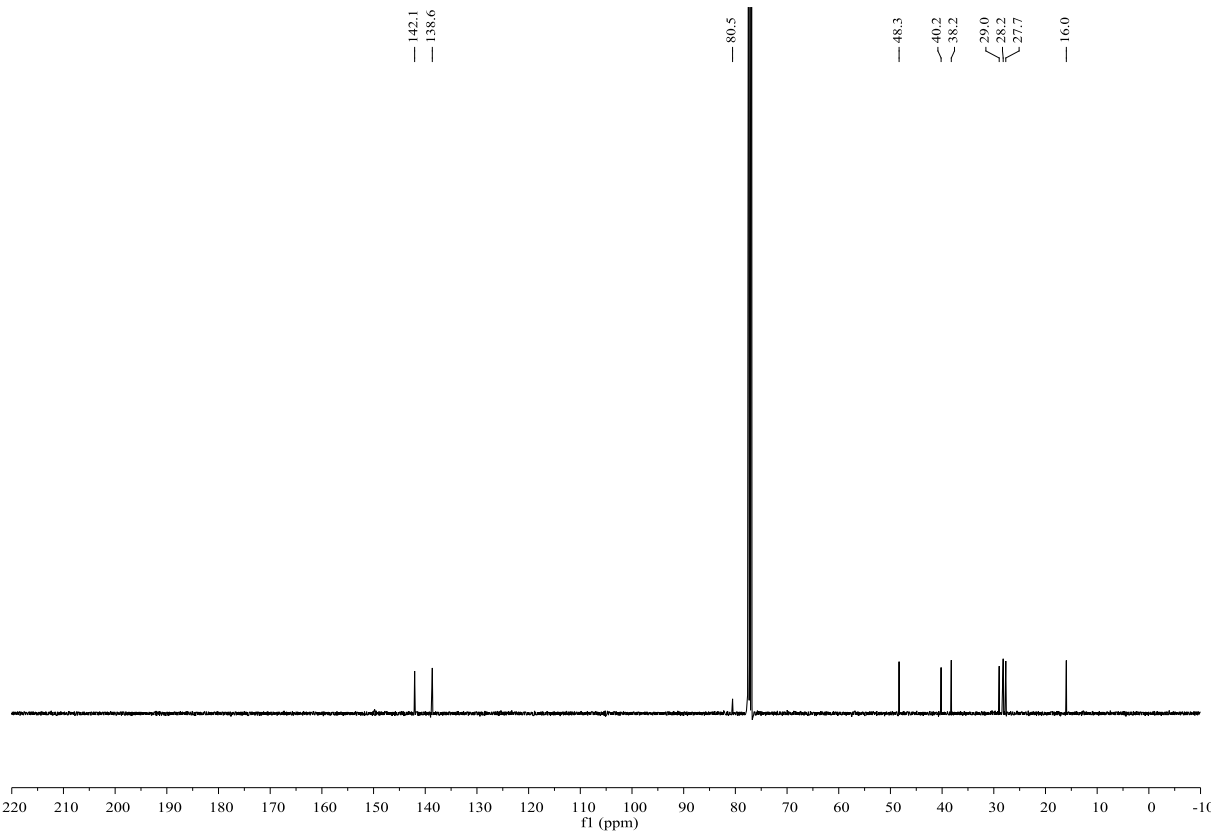
569 (^{13}C NMR, 150 MHz, $CDCl_3$)



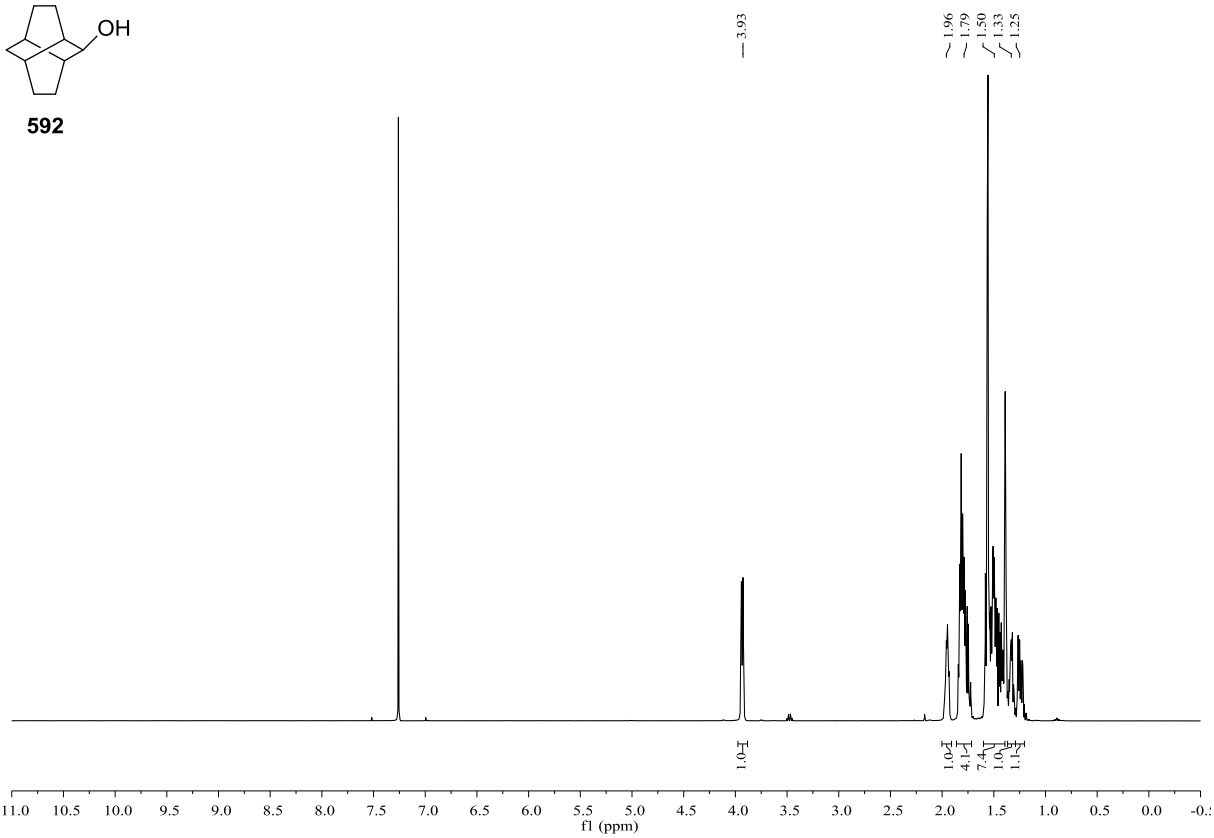
591 (^{1}H NMR, 400 MHz, $CDCl_3$)



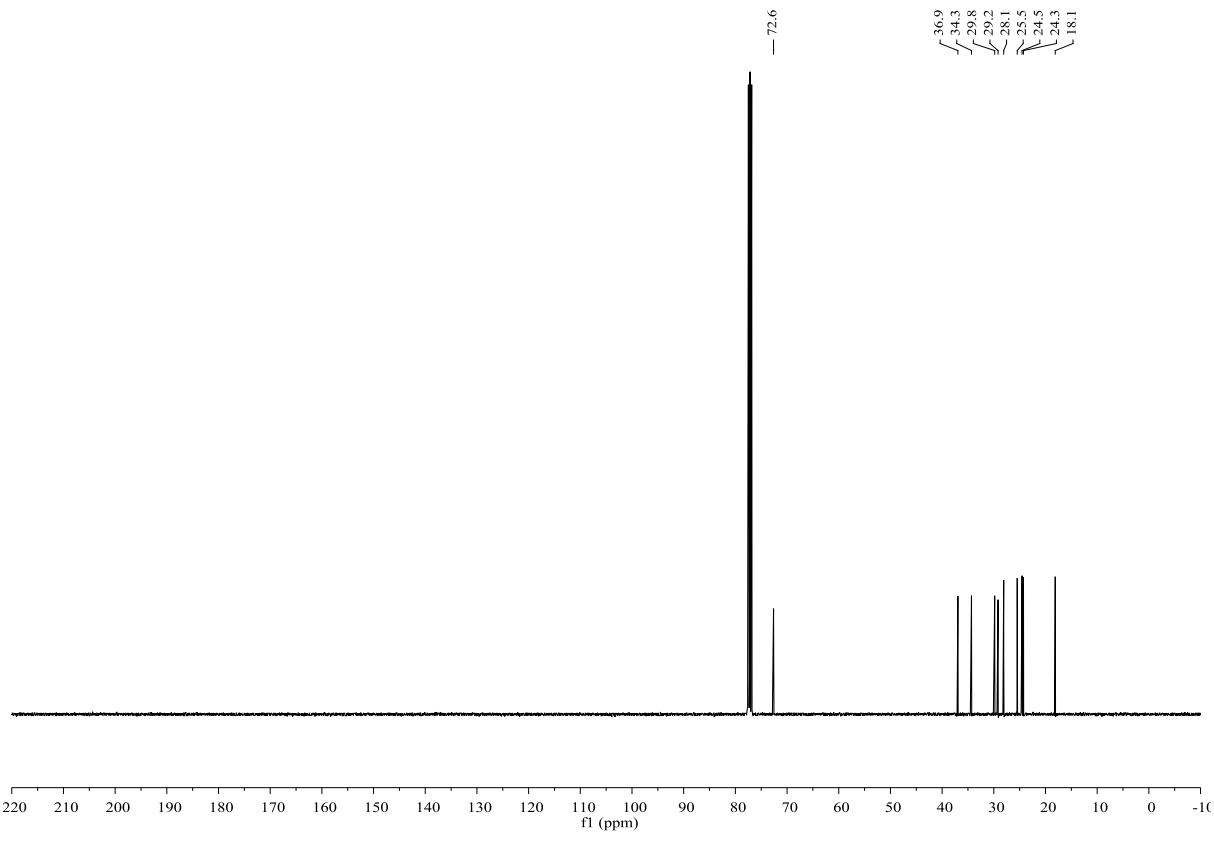
591 (^{13}C NMR, 100 MHz, $CDCl_3$)



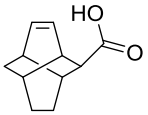
592 (^{1}H NMR, 400 MHz, $CDCl_3$)



592 (^{13}C NMR, 100 MHz, $CDCl_3$)

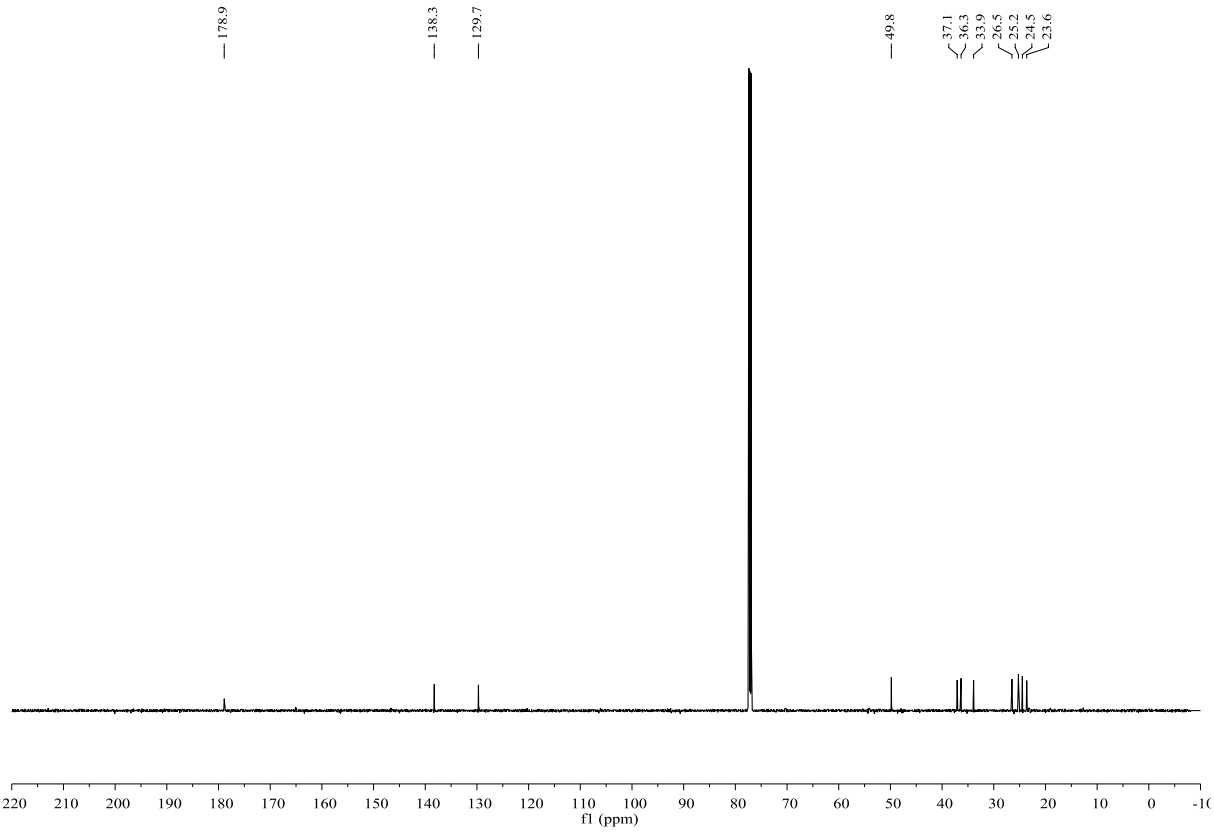


597 (^{1}H NMR, 600 MHz, $CDCl_3$)

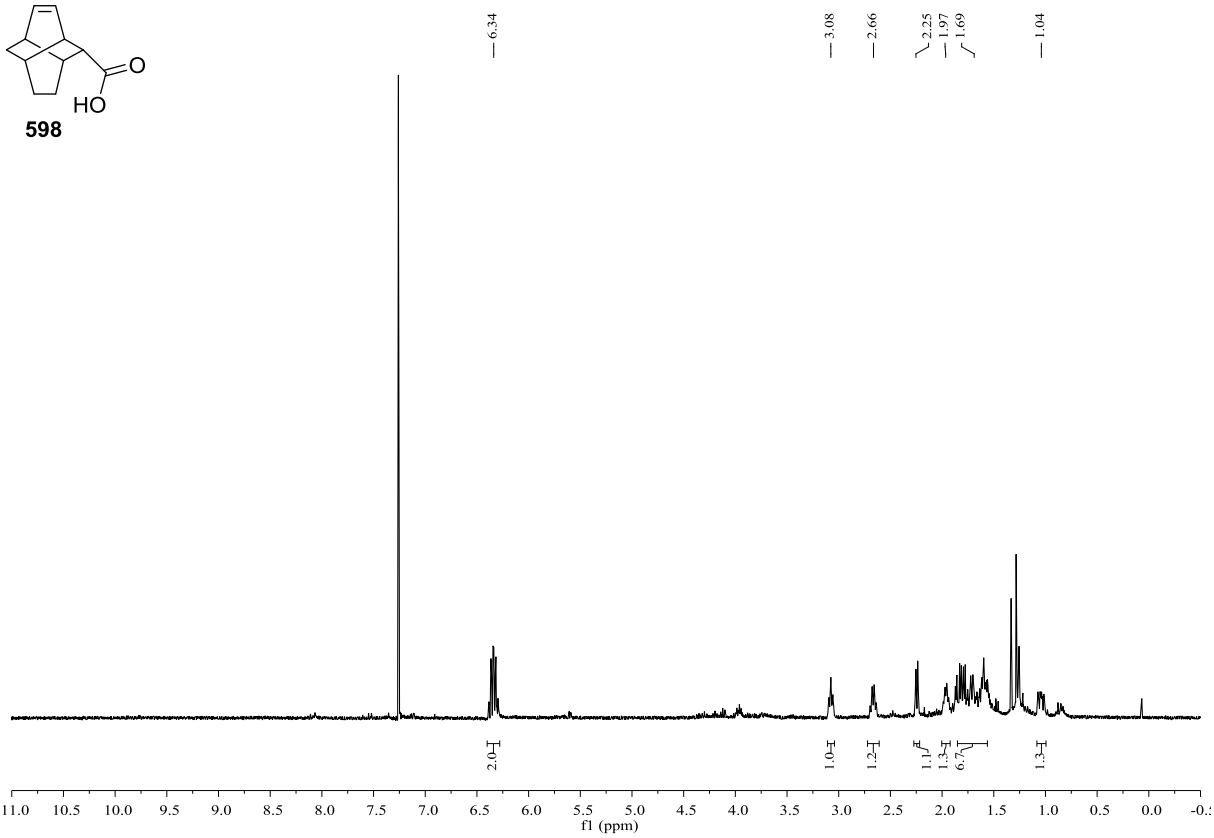


597

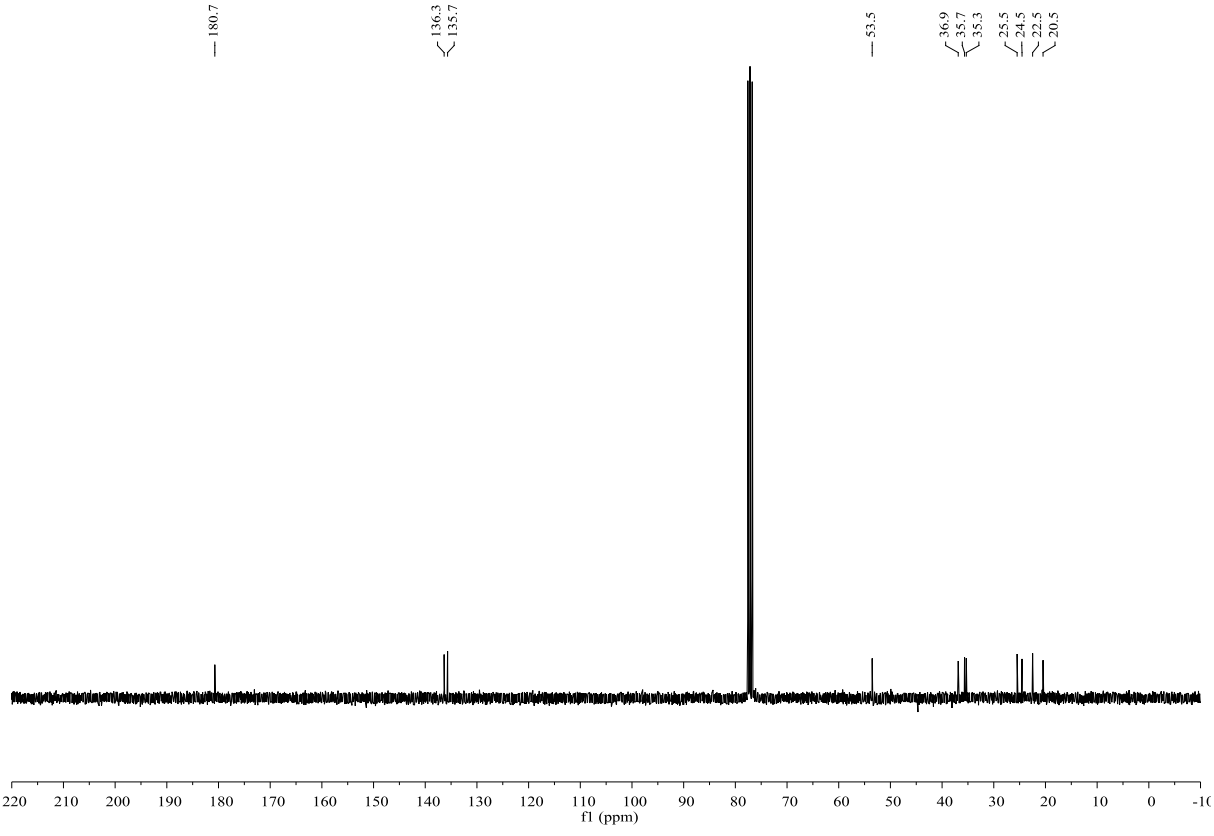
597 (^{13}C NMR, 150 MHz, $CDCl_3$)



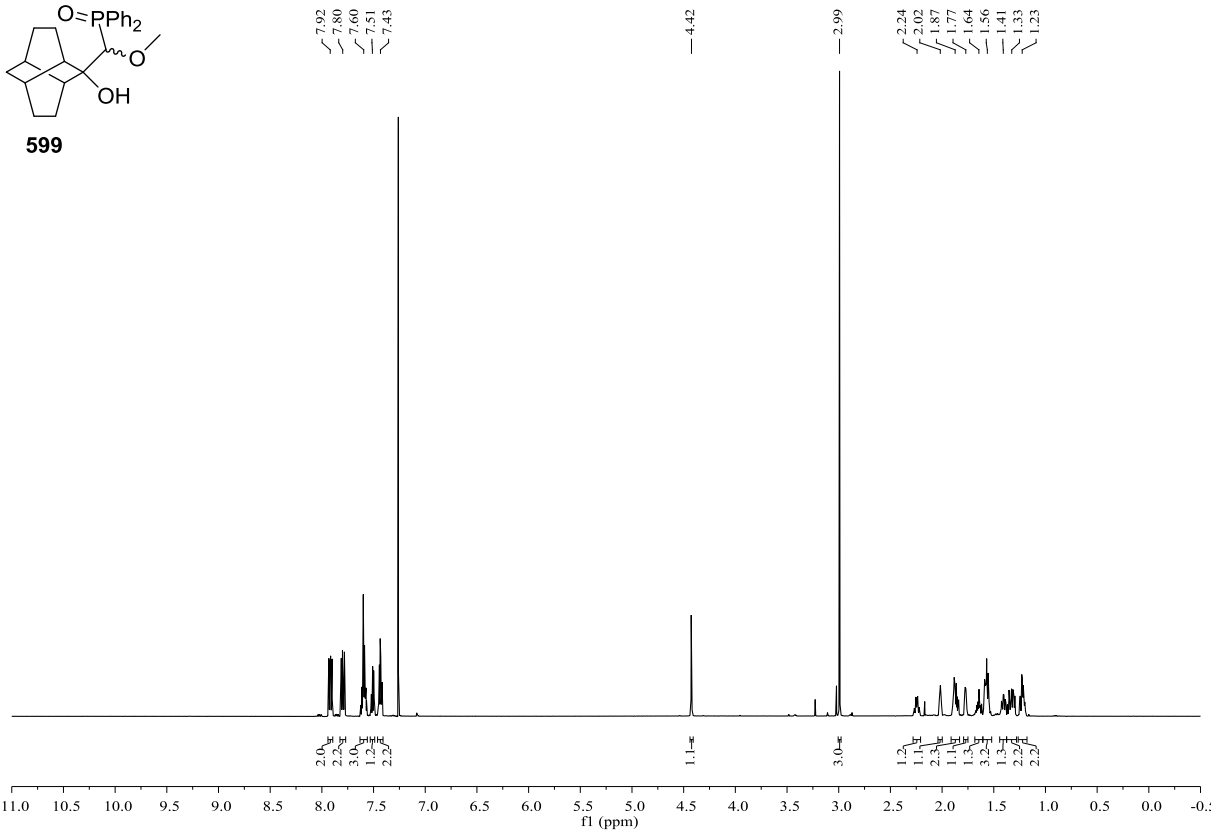
598 (^{1}H NMR, 300 MHz, $CDCl_3$)



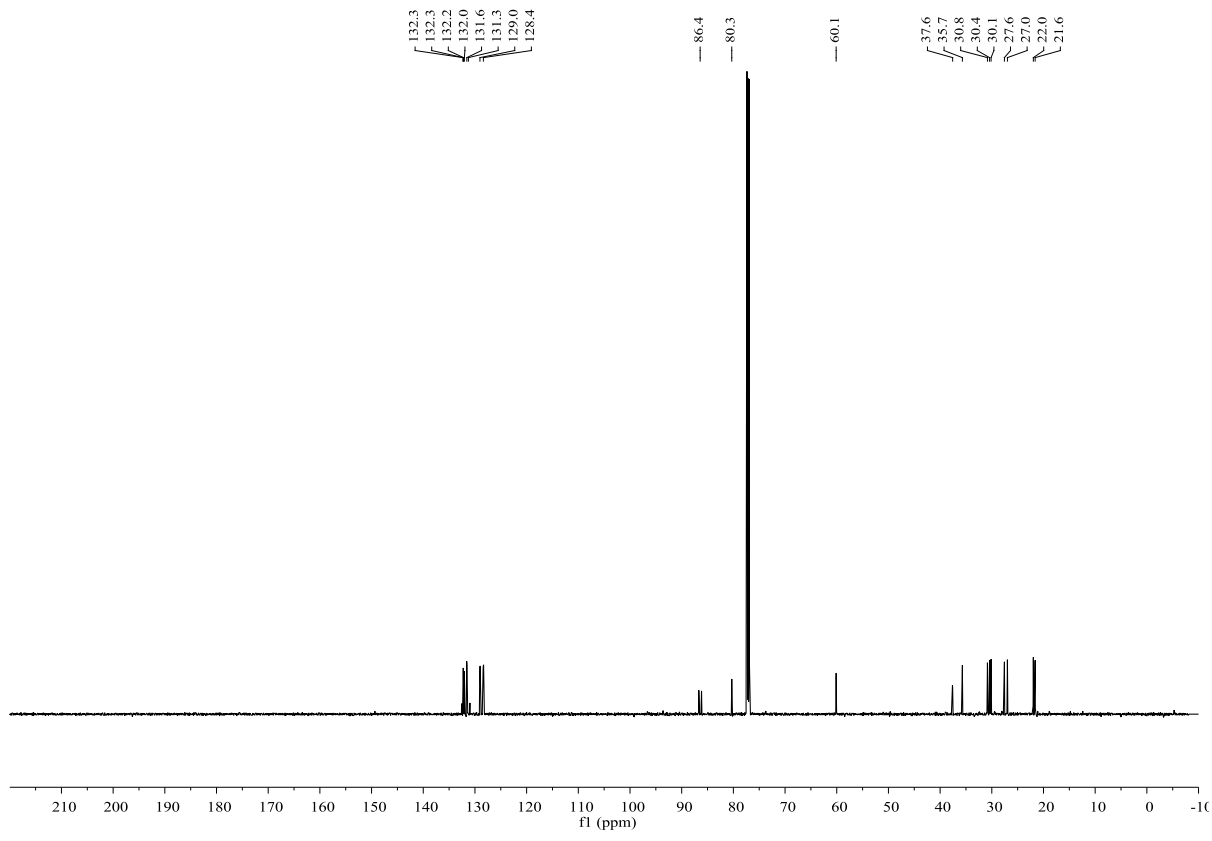
598 (^{13}C NMR, 75 MHz, $CDCl_3$)



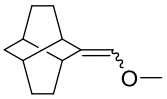
599 (^{1}H NMR, 600 MHz, $CDCl_3$)



599 (^{13}C NMR, 150 MHz, $CDCl_3$)

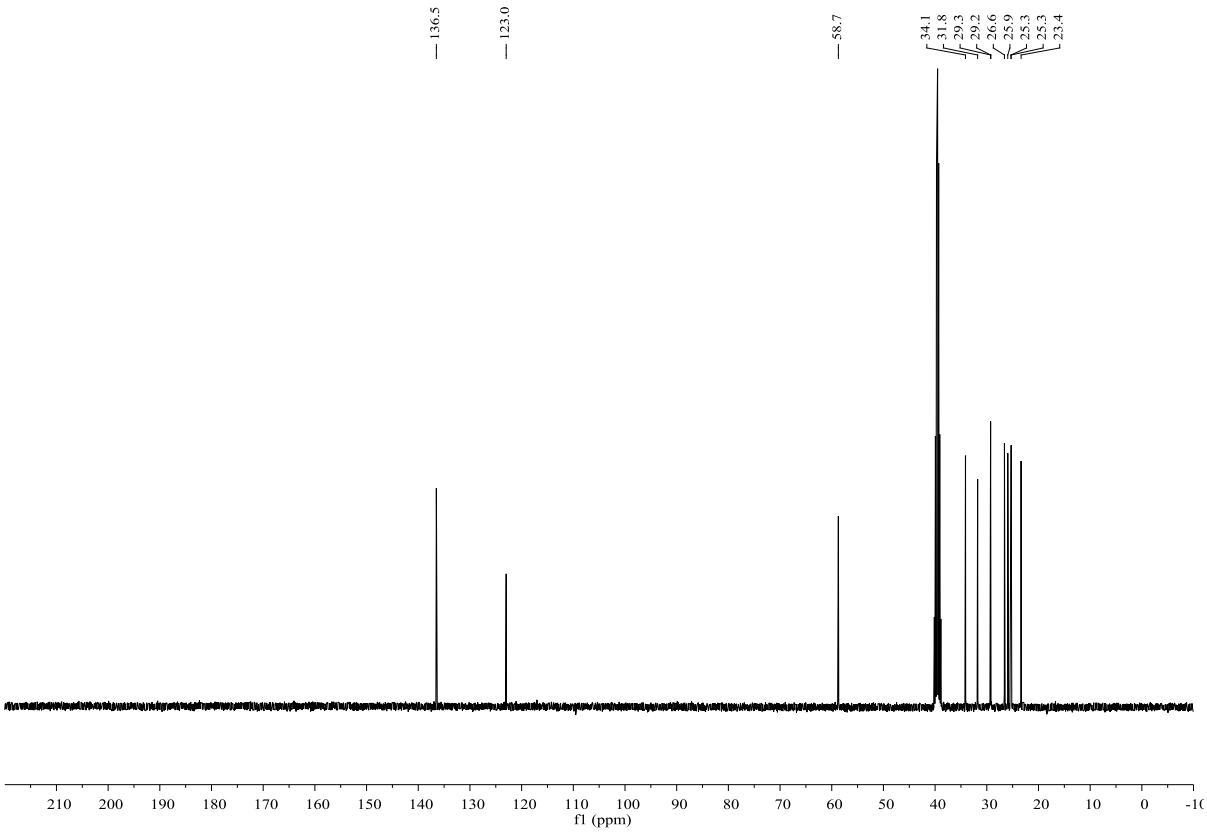


600 (^{1}H NMR, 400 MHz, DMSO-d_6)

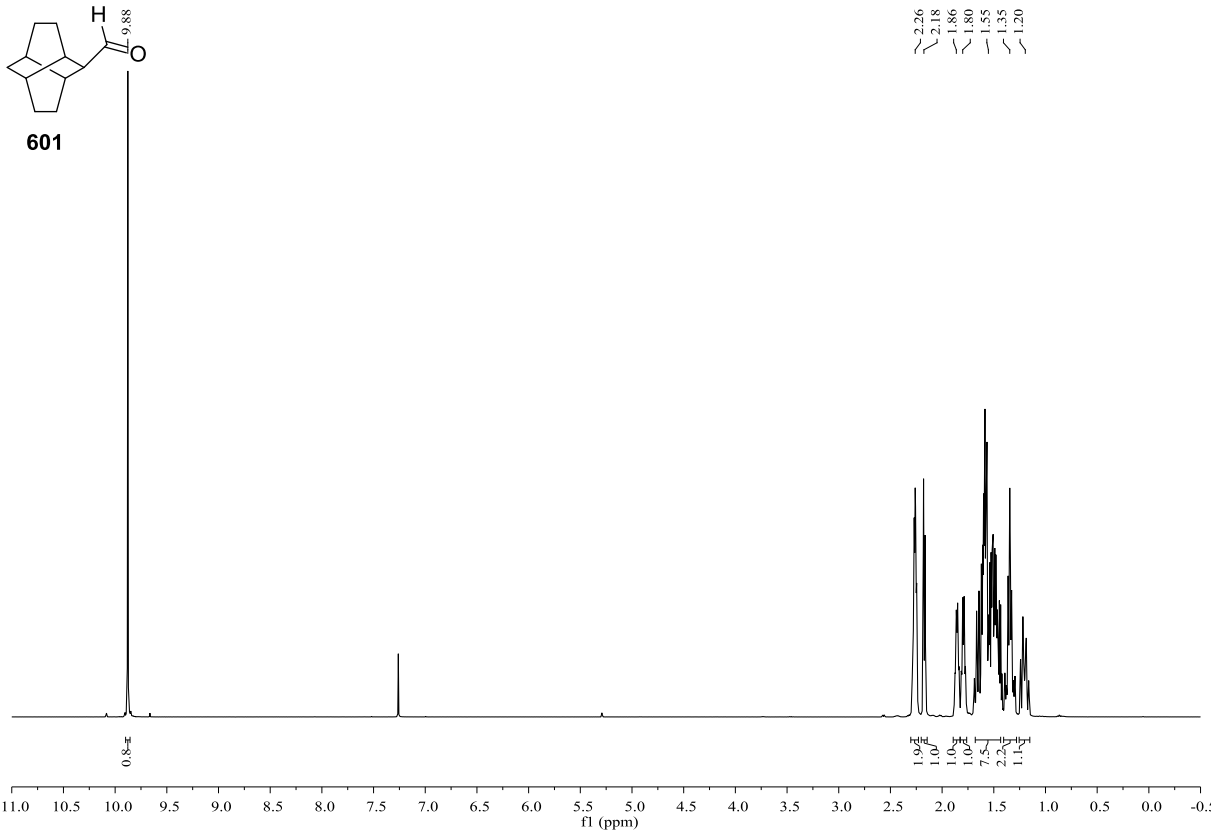


600

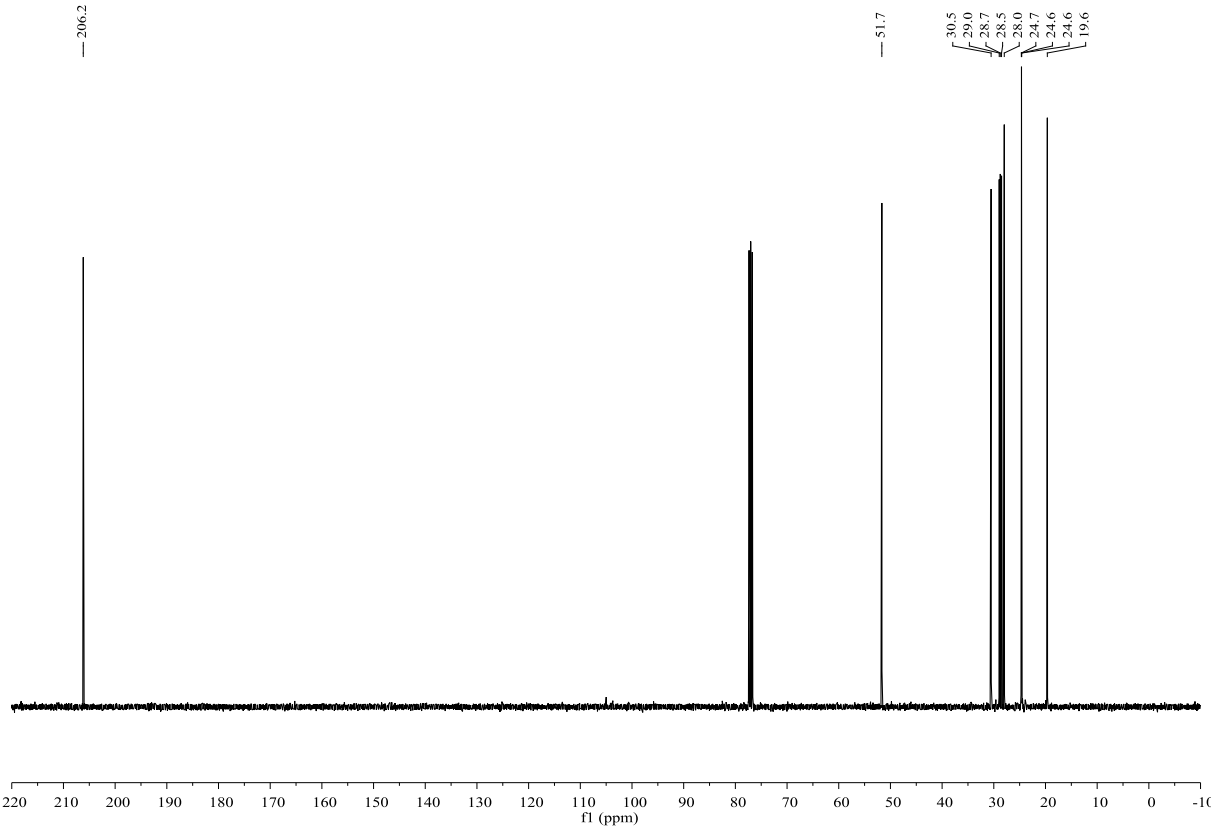
600 (^{13}C NMR, 100 MHz, DMSO-d_6)



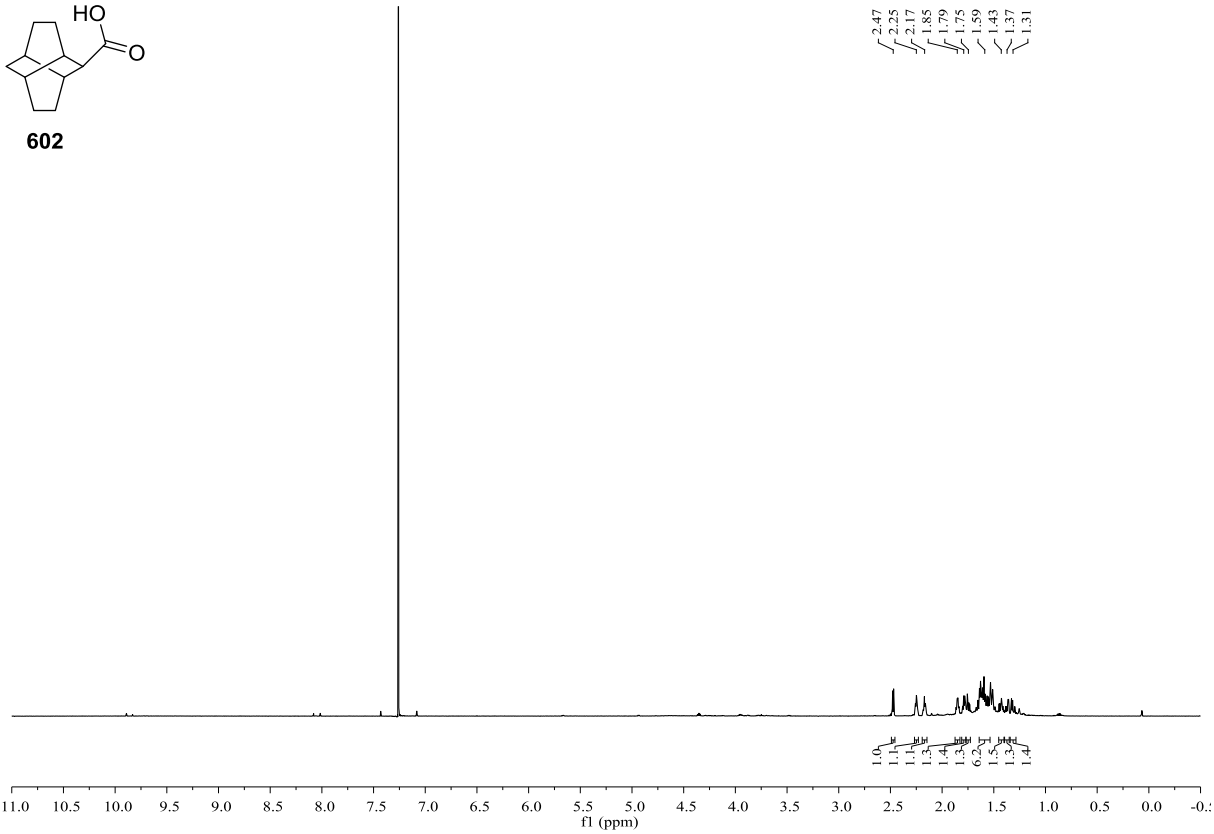
601 (^{1}H NMR, 400 MHz, $CDCl_3$)



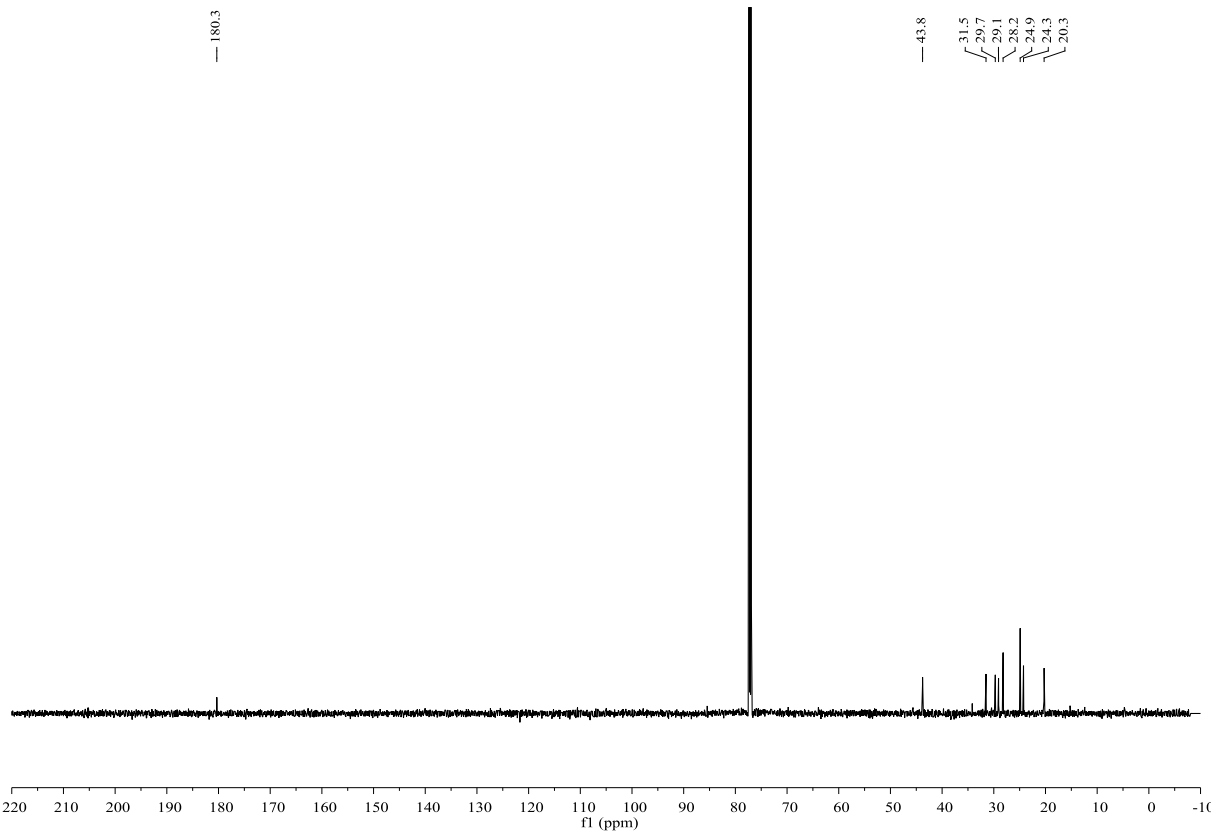
601 (^{13}C NMR, 100 MHz, $CDCl_3$)



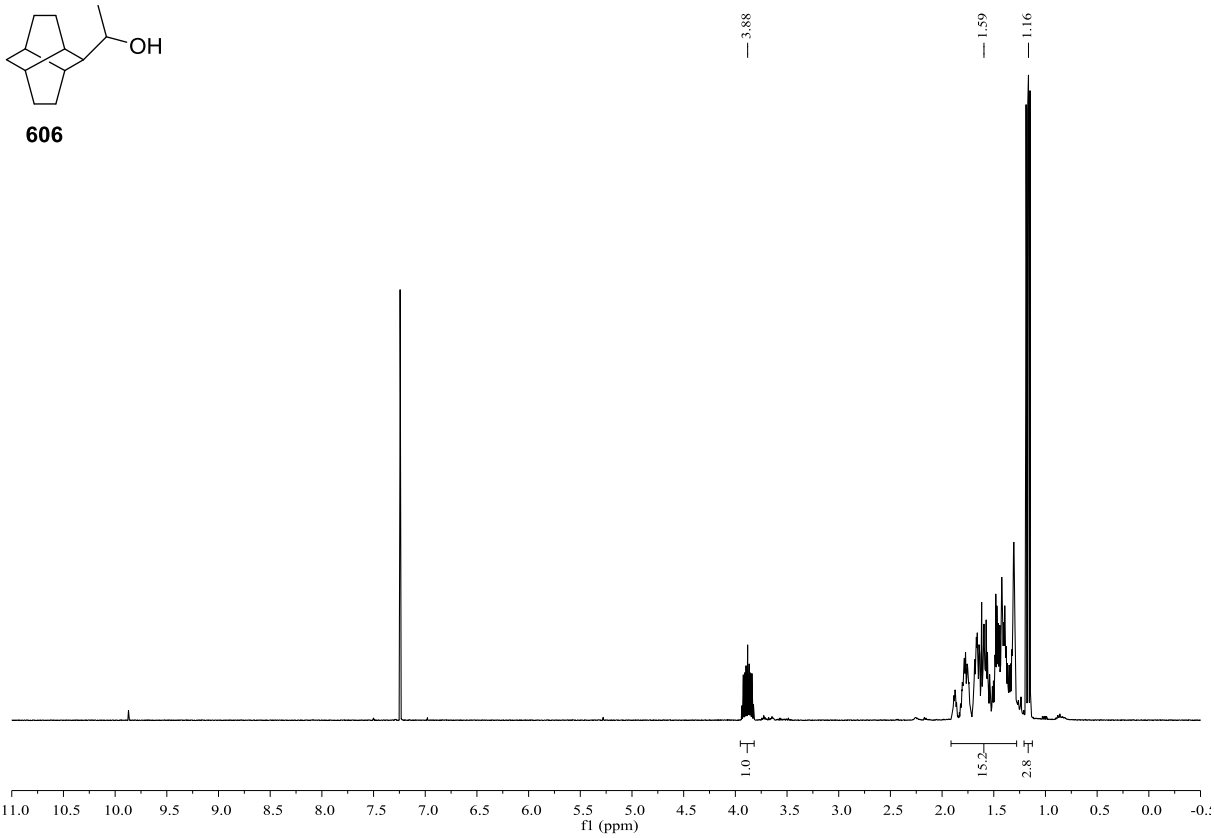
602 (^{1}H NMR, 600 MHz, $CDCl_3$)



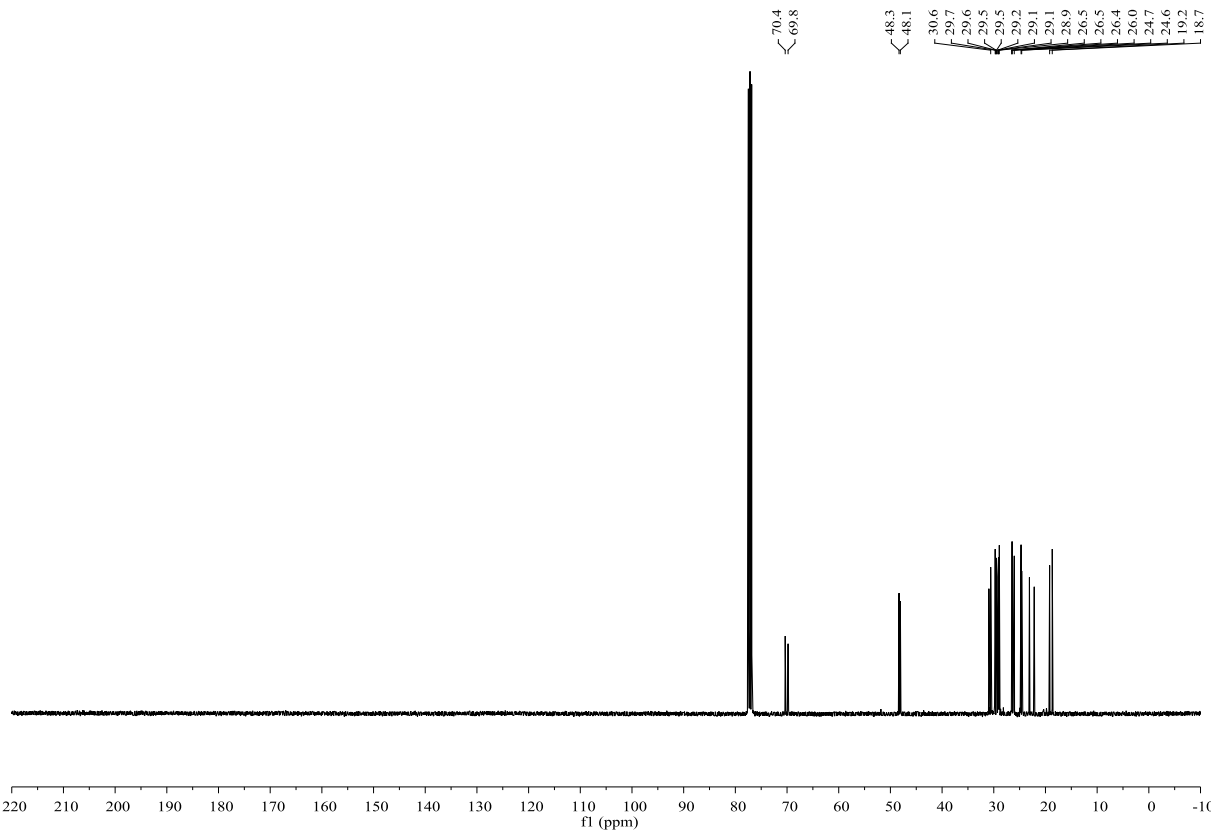
602 (^{13}C NMR, 150 MHz, $CDCl_3$)



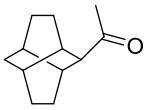
606 (^{1}H NMR, 400 MHz, $CDCl_3$)



606 (^{13}C NMR, 100 MHz, $CDCl_3$)

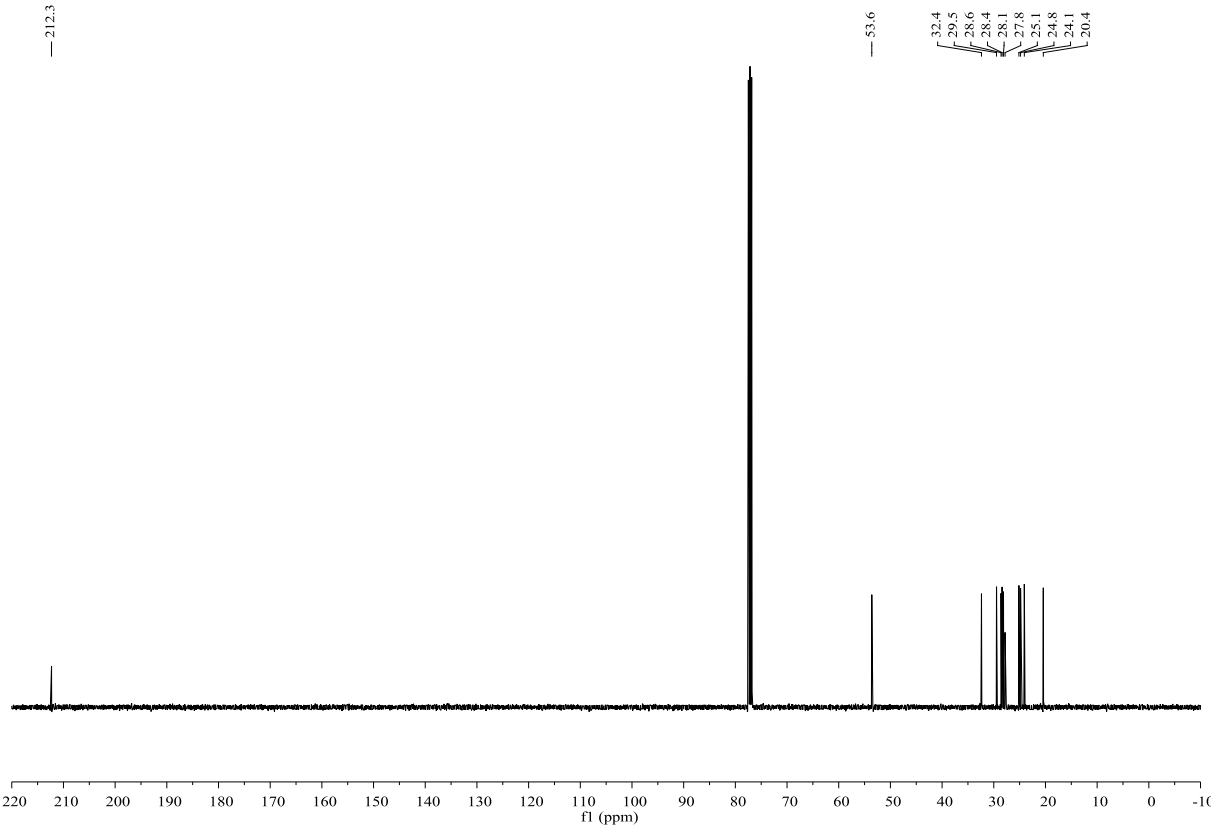


607 (^{1}H NMR, 400 MHz, $CDCl_3$)

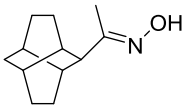


607

607 (^{13}C NMR, 100 MHz, $CDCl_3$)

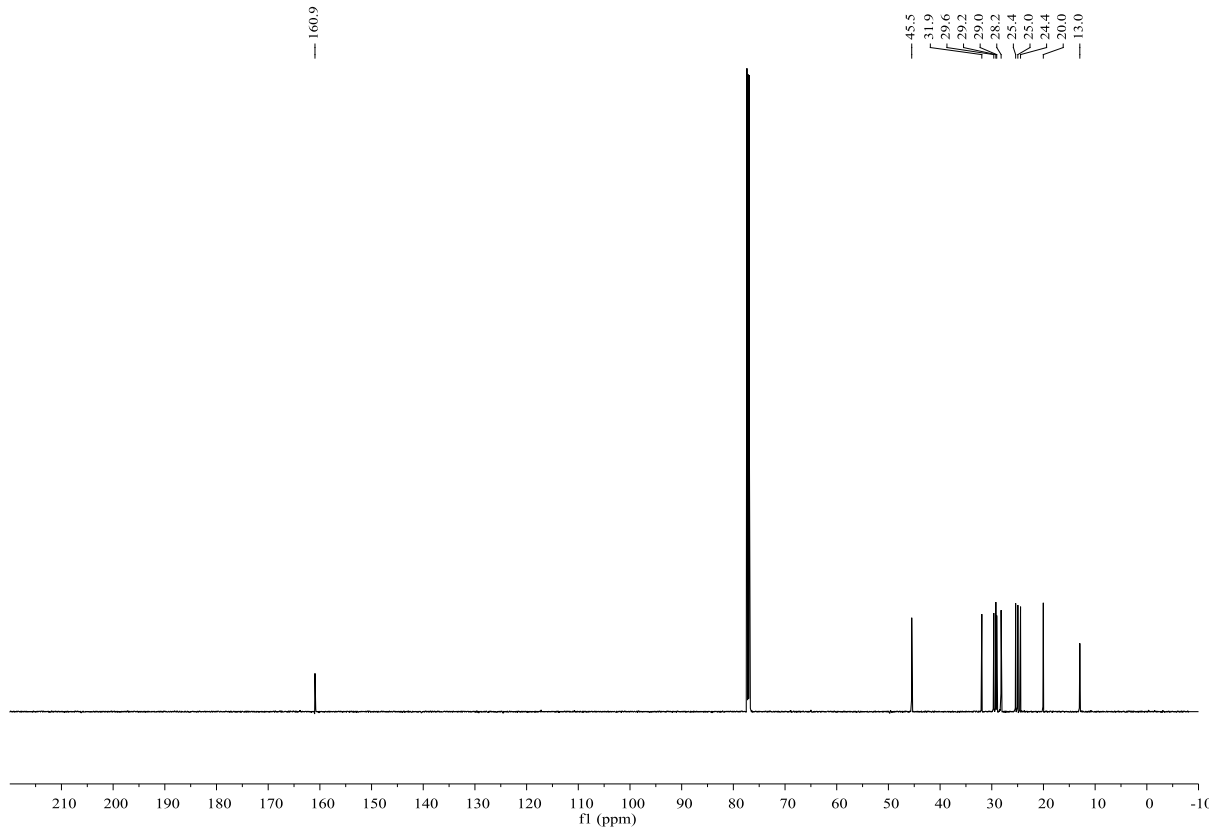


608 (^{1}H NMR, 600 MHz, $CDCl_3$)

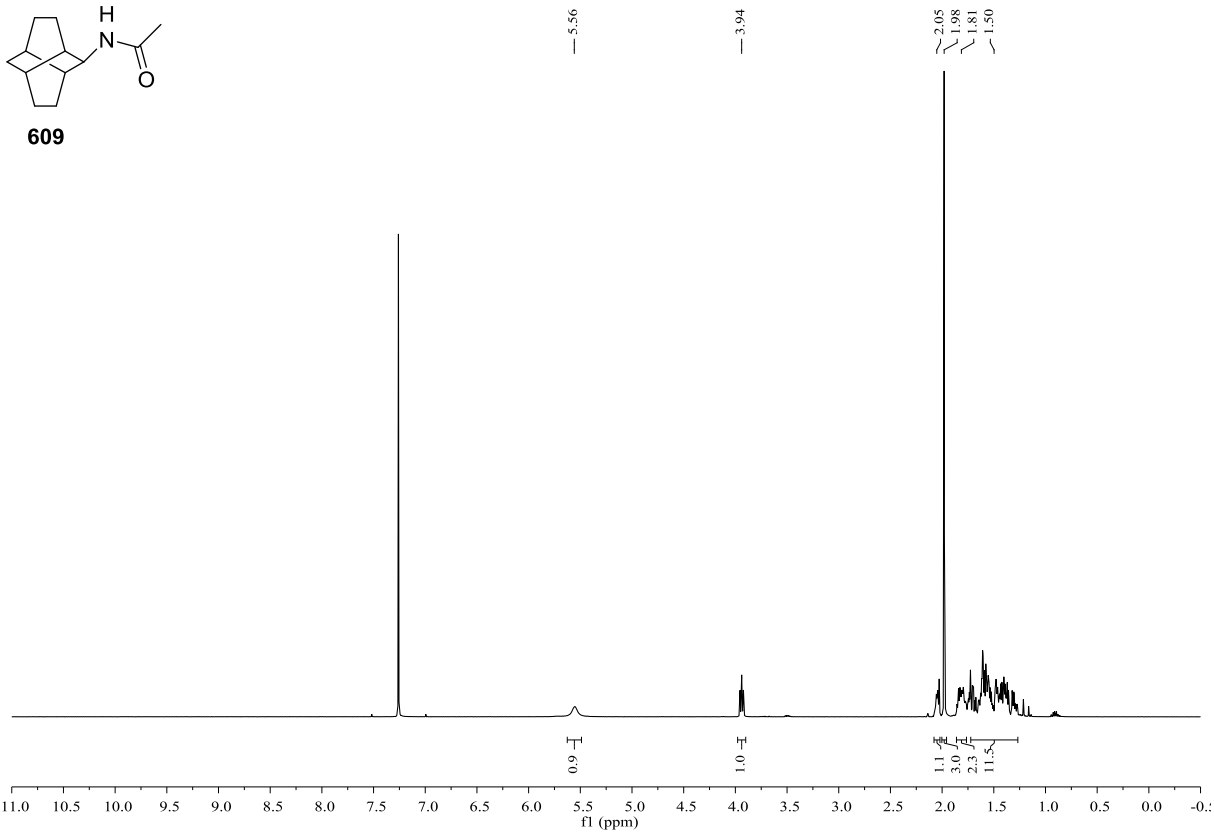


608

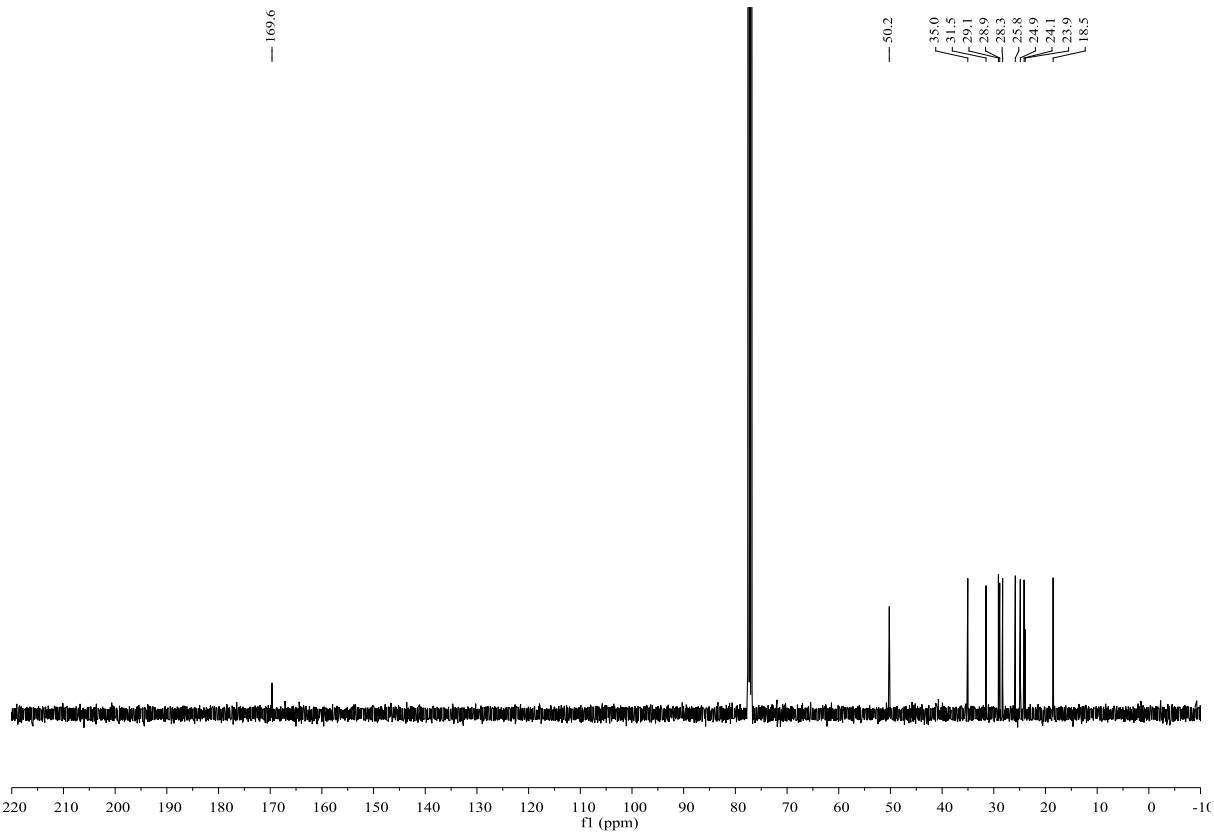
608 (^{13}C NMR, 150 MHz, $CDCl_3$)



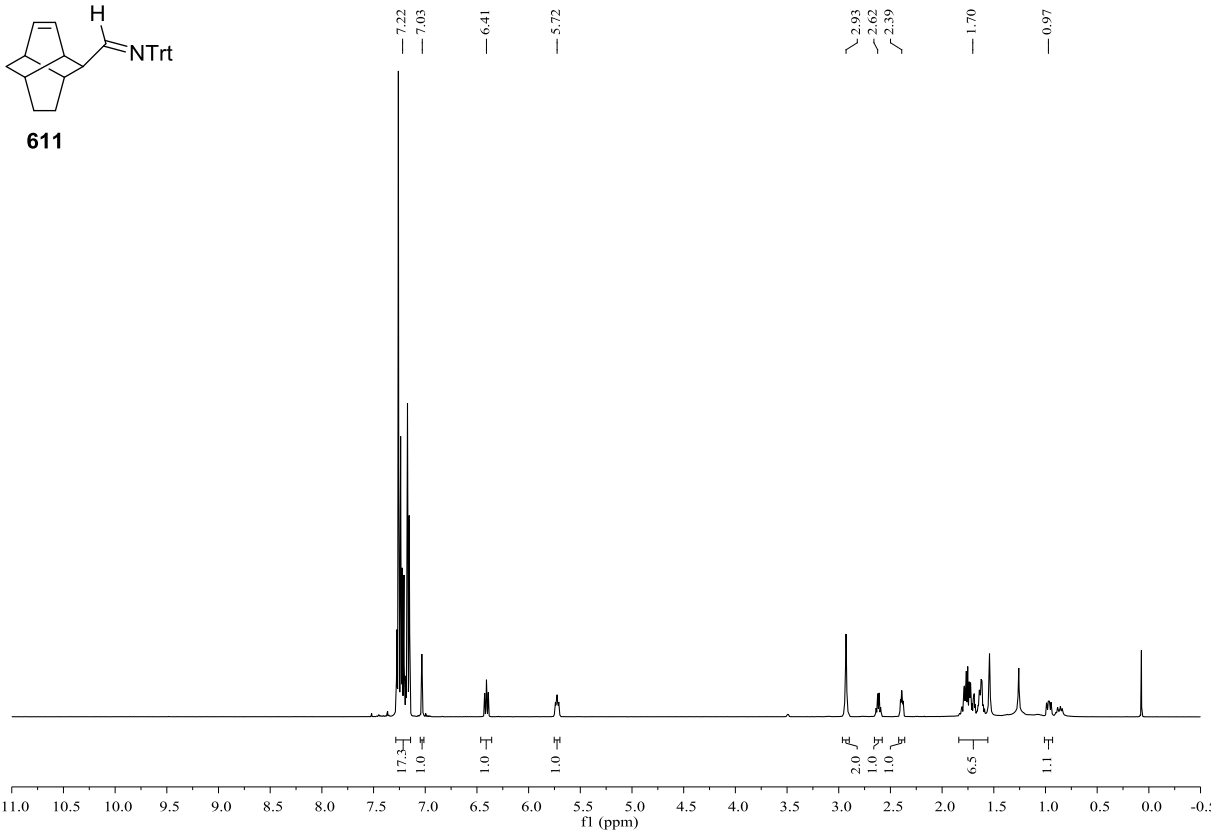
609 (^{1}H NMR, 400 MHz, $CDCl_3$)



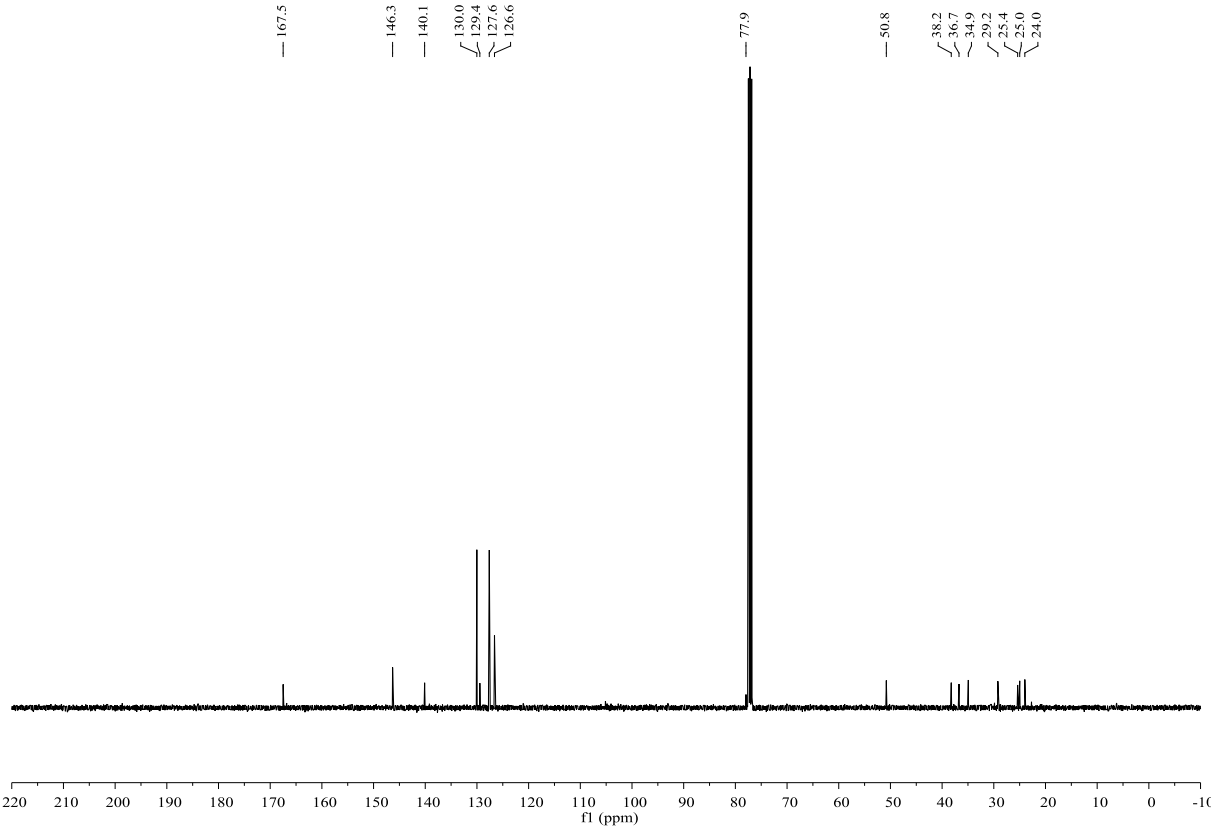
609 (^{13}C NMR, 100 MHz, $CDCl_3$)



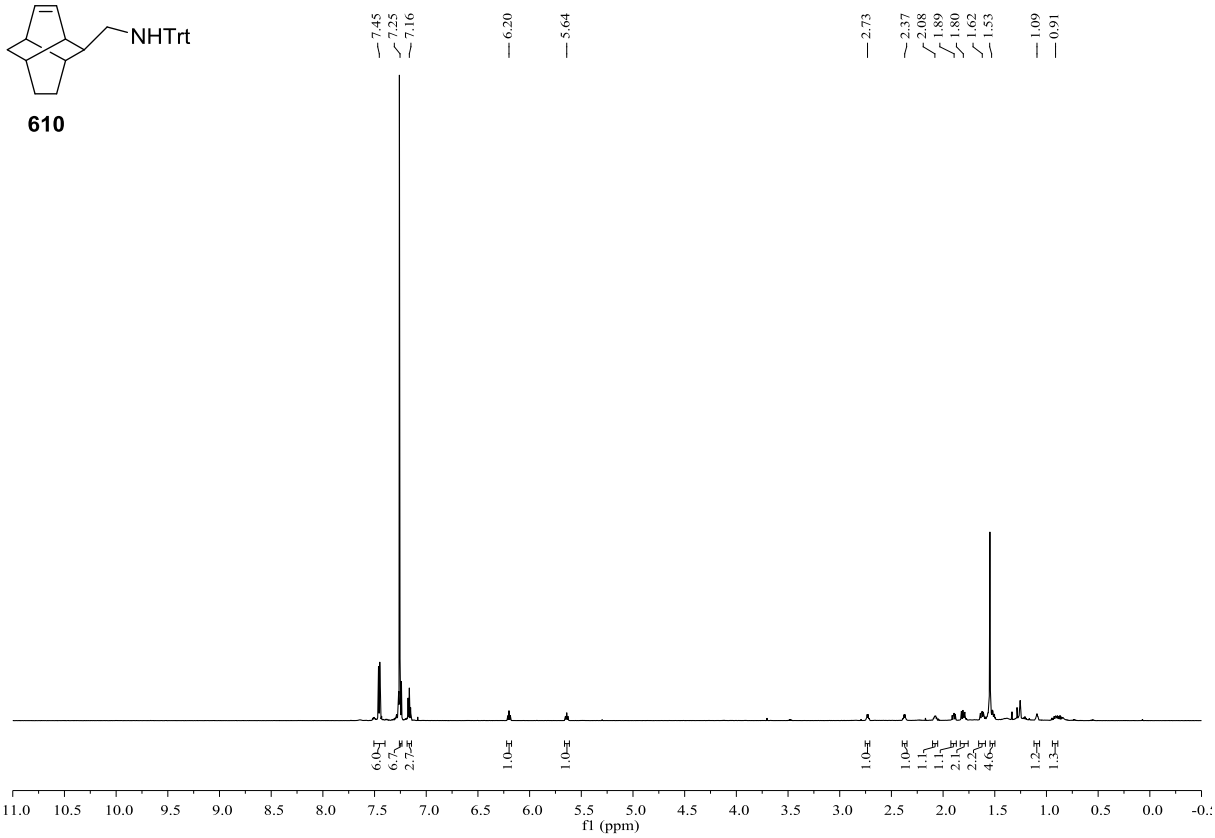
611 (^{1}H NMR, 400 MHz, $CDCl_3$)



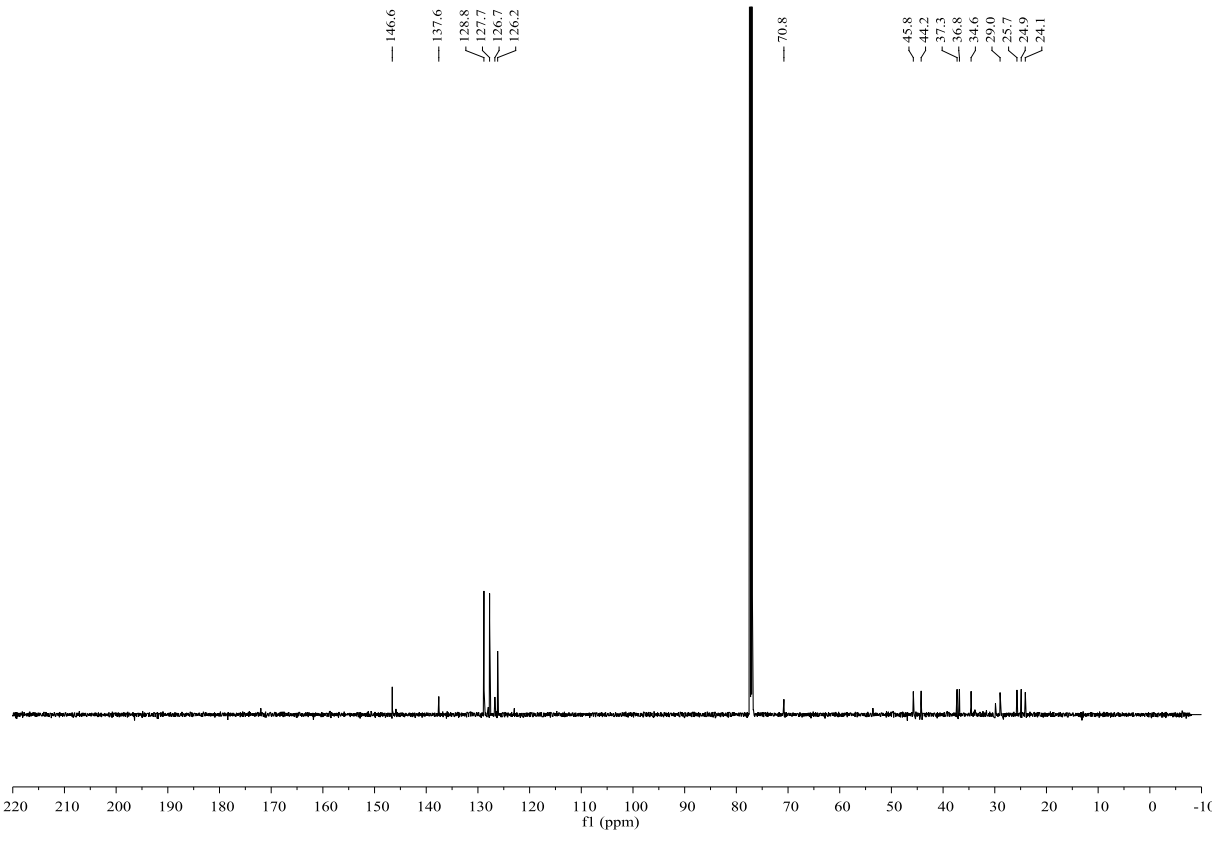
611 (^{13}C NMR, 100 MHz, $CDCl_3$)



610 (^{1}H NMR, 600 MHz, $CDCl_3$)



610 (^{13}C NMR, 150 MHz, $CDCl_3$)



9 Crystallographic Data

Crystallographic data for published compounds has also been deposited at the CCDC. Figure 35 gives an overview of the molecular structures together with the CCDC numbers for published structures. After the relevant crystallographic and refinement data an ORTEP drawing of the respective X-ray structure is given which shows, in case of disordered structures, the major part. Thermal ellipsoids are scaled to 50% probability. Hydrogen atoms are displayed in arbitrary size. The following color code is used for the X-ray structures: aquamarine = Cl; black = H; blue = N; brown = Br; navy = Pd; orange = P; gray = C; red = O; violet = I; yellow = S.

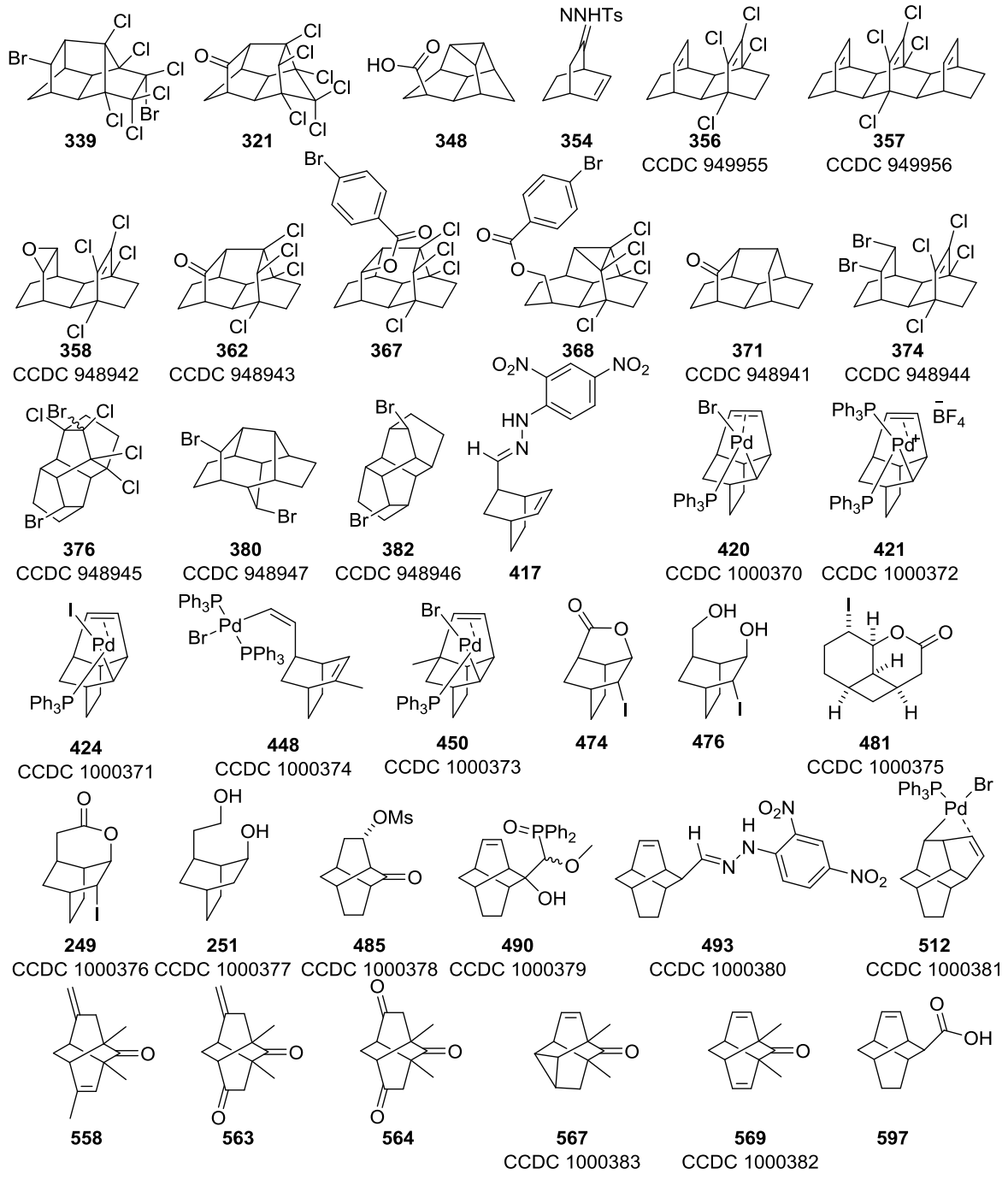


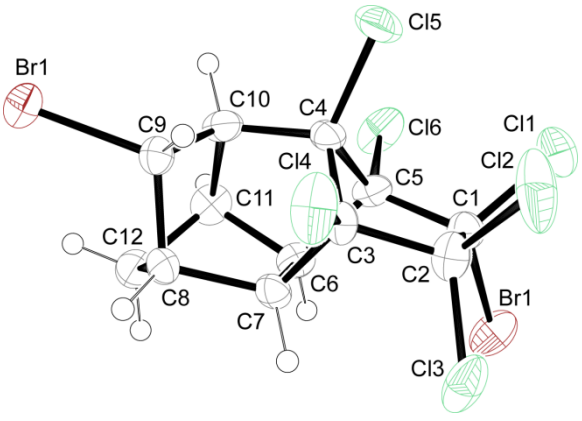
Figure 35. Compounds which have been characterized by single crystal X-ray diffraction.

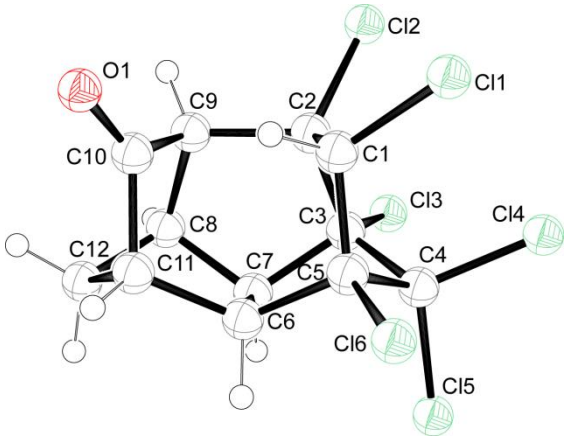
339

net formula	$C_{12}H_8Br_2Cl_6$
M_r/g mol^{-1}	524.716
crystal size/mm	0.16 × 0.07 × 0.02
T/K	173(2)
radiation	MoKα
diffractometer	'KappaCCD'
crystal system	monoclinic
space group	*Cc*
a/Å	8.5211(4)
b/Å	24.6935(11)
c/Å	7.8078(4)
α/°	90
β/°	109.182(3)
γ/°	90
V/Å^3	1551.67(13)
Z	4
calc. density/g cm^{-3}	2.24616(19)
μ/mm^{-1}	6.241
absorption correction	multi-scan
transmission factor range	0.5264–0.7087
refls. measured	10726
R_{int}	0.0445
mean σ(I)/I	0.0382
θ range	3.18–25.35
observed refls.	2527
x, y (weighting scheme)	0.0377, 2.4246
hydrogen refinement	constr
Flack parameter	−0.005(9)
refls in refinement	2677
parameters	181
restraints	2
$R(F_{obs})$	0.0293
$R_w(F^2)$	0.0727
S	1.040
shift/error$_{max}$	0.001
max electron density/e Å^{-3}	0.444
min electron density/e Å^{-3}	−0.403

321

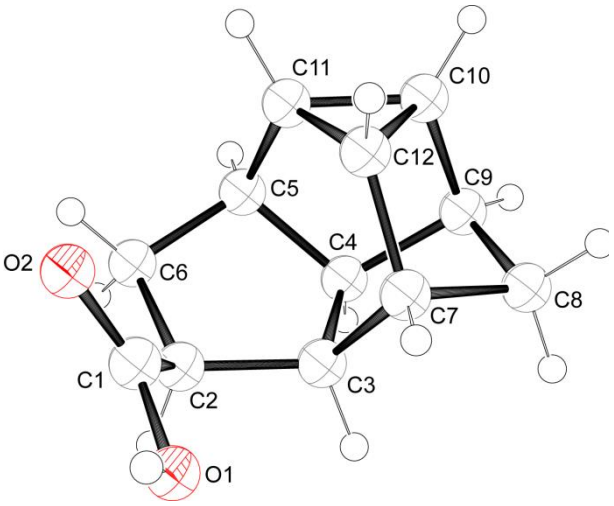
net formula	$C_{12}H_8Cl_6O$
M_r/g mol^{-1}	380.908
crystal size/mm	0.17 × 0.12 × 0.09
T/K	173(2)
radiation	MoKα
diffractometer	'KappaCCD'
crystal system	monoclinic
space group	$P2_1/n$
a/Å	8.2741(2)
b/Å	11.5947(3)
c/Å	14.1198(3)
α/°	90
β/°	92.1715(14)
γ/°	90
V/Å^3	1353.62(5)
Z	4
calc. density/g cm^{-3}	1.86912(7)
μ/mm^{-1}	1.254
absorption correction	none
refls. measured	11095
R_{int}	0.0308
mean σ(I)/I	0.0239
θ range	3.31–27.47
observed refls.	2849
x, y (weighting scheme)	0.0439, 5.3007
hydrogen refinement	constr
refls in refinement	3092
parameters	172
restraints	0
$R(F_{obs})$	0.0546
$R_w(F^2)$	0.1305
S	1.103
shift/error$_{max}$	0.001
max electron density/e Å^{-3}	2.169
min electron density/e Å^{-3}	−0.601





348

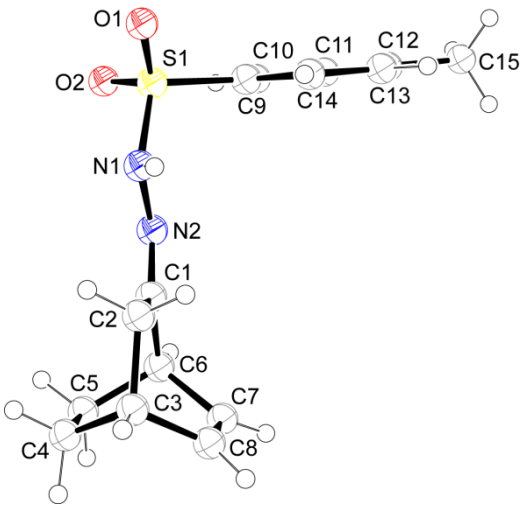
net formula	$C_{12}H_{14}O_2$
M_r/g mol^{-1}	190.238
crystal size/mm	0.29 × 0.08 × 0.07
T/K	173(2)
radiation	MoKα
diffractometer	'Oxford XCalibur'
crystal system	triclinic
space group	P1bar
a/Å	6.4796(4)
b/Å	13.0144(10)
c/Å	16.7513(14)
α/°	100.050(7)
β/°	91.697(6)
γ/°	96.712(6)
V/Å^3	1379.59(18)
Z	6
calc. density/g cm^{-3}	1.37390(18)
μ/mm^{-1}	0.092
absorption correction	'multi-scan'
transmission factor range	0.85870–1.00000
refls. measured	9035
R_{int}	0.0528
mean σ(I)/I	0.1405
θ range	4.22–25.25
observed refls.	2595
x, y (weighting scheme)	0.1327, 0
hydrogen refinement	constr
refls in refinement	4961
parameters	382
restraints	0
$R(F_{obs})$	0.0840
$R_w(F^2)$	0.2366
S	0.976
shift/error$_{max}$	0.001
max electron density/e Å^{-3}	0.549
min electron density/e Å^{-3}	−0.249



354

net formula	$C_{15}H_{18}N_2O_2S$
M_r/g mol^{-1}	290.382
crystal size/mm	0.32 × 0.28 × 0.11
T/K	173(2)
radiation	MoKα
diffractometer	'Oxford XCalibur'
crystal system	triclinic
space group	P1bar
a/Å	6.4466(10)
b/Å	10.7096(15)
c/Å	11.4546(18)
α/°	70.068(14)
β/°	74.320(13)
γ/°	78.864(12)
V/Å^3	711.32(19)
Z	2
calc. density/g cm^{-3}	1.3558(4)
μ/mm^{-1}	0.231
absorption correction	'multi-scan'
transmission factor range	0.81938–1.00000
refls. measured	4785
R_{int}	0.0314
mean σ(I)/I	0.0460
θ range	4.26–26.37
observed refls.	2388
x, y (weighting scheme)	0.0498, 0.3318
hydrogen refinement	mixed
refls in refinement	2894
parameters	186
restraints	0
$R(F_{obs})$	0.0450
$R_w(F^2)$	0.1203
S	1.033
shift/error$_{max}$	0.001
max electron density/e Å^{-3}	0.299
min electron density/e Å^{-3}	−0.375

C-bound H: constr, N-bound H: refall.

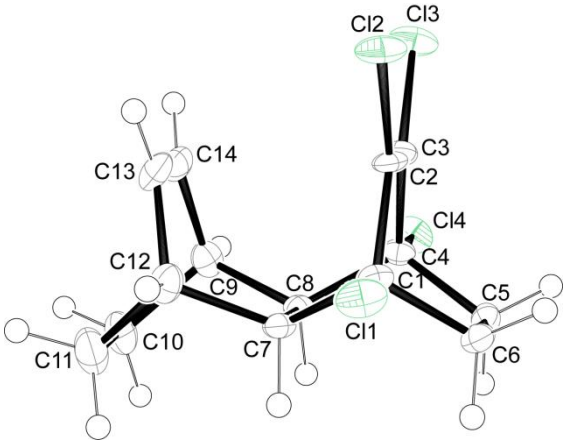


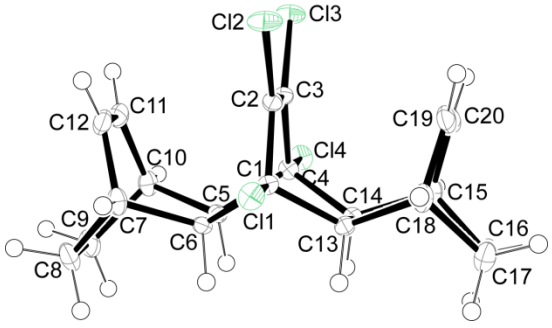
356

CCDC number	949955
net formula	$C_{14}H_{14}Cl_4$
M_r/g mol^{-1}	324.072
crystal size/mm	0.096 × 0.049 × 0.023
T/K	123(2)
radiation	'Mo Kα
diffractometer	'Bruker D8Venture'
crystal system	triclinic
space group	P1bar
a/Å	7.0652(8)
b/Å	8.2217(9)
c/Å	13.0265(14)
α/°	92.900(3)
β/°	90.127(3)
γ/°	114.750(3)
V/Å^3	686.07(13)
Z	2
calc. density/g cm^{-3}	1.5688(3)
μ/mm^{-1}	0.840
absorption correction	multi-scan
transmission factor range	0.8682–0.9582
refls. measured	9118
R_{int}	0.0629
mean σ(I)/I	0.0579
θ range	3.07–25.36
observed refls.	1889
x, y (weighting scheme)	0.0277, 0.2364
hydrogen refinement	constr
refls in refinement	2522
parameters	163
restraints	0
$R(F_{obs})$	0.0360
$R_w(F^2)$	0.0750
S	1.033
shift/error$_{max}$	0.001
max electron density/e Å^{-3}	0.361
min electron density/e Å^{-3}	−0.284

357

CCDC number	949956
net formula	$C_{20}H_{20}Cl_4$
M_r/g mol^{-1}	402.184
crystal size/mm	0.151 × 0.089 × 0.081
T/K	123(2)
radiation	'Mo Kα
diffractometer	'Bruker D8Venture'
crystal system	triclinic
space group	P1bar
a/Å	7.0286(4)
b/Å	8.7167(5)
c/Å	15.6853(9)
α/°	83.186(2)
β/°	87.4669(19)
γ/°	66.2540(16)
V/Å^3	873.40(9)
Z	2
calc. density/g cm^{-3}	1.52931(16)
μ/mm^{-1}	0.677
absorption correction	multi-scan
transmission factor range	0.9197–0.9582
refls. measured	8310
R_{int}	0.0244
mean σ(I)/I	0.0296
θ range	3.17–25.03
observed refls.	2728
x, y (weighting scheme)	0.0276, 0.7769
hydrogen refinement	constr
refls in refinement	3057
parameters	217
restraints	0
$R(F_{obs})$	0.0299
$R_w(F^2)$	0.0766
S	1.116
shift/error$_{max}$	0.001
max electron density/e Å^{-3}	0.364
min electron density/e Å^{-3}	−0.227

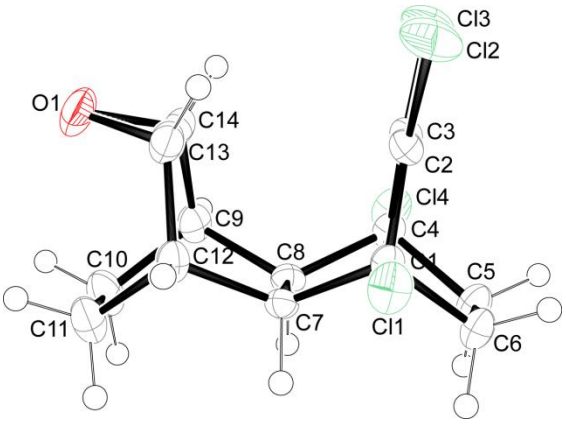




358

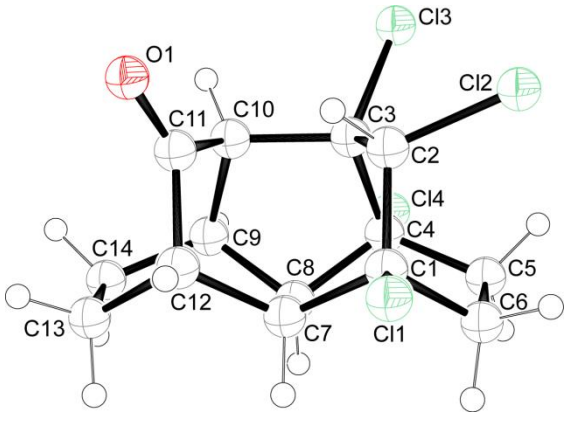
CCDC number	948942
net formula	$C_{14}H_{14}Cl_4O$
M_r/g mol^{-1}	340.071
crystal size/mm	0.16 × 0.09 × 0.06
T/K	173(2)
radiation	MoKα
diffractometer	'KappaCCD'
crystal system	orthorhombic
space group	$P2_12_12_1$
a/Å	8.8558(2)
b/Å	12.1899(3)
c/Å	12.9536(3)
α/°	90
β/°	90
γ/°	90
V/Å^3	1398.36(6)
Z	4
calc. density/g cm^{-3}	1.61535(7)
μ/mm^{-1}	0.834
absorption correction	none
refls. measured	11150
R_{int}	0.0297
mean σ(I)/I	0.0279
θ range	3.15–27.43
observed refls.	2936
x, y (weighting scheme)	0.0313, 0.5754
hydrogen refinement	constr
Flack parameter	0.40(7)
refls in refinement	3189
parameters	173
restraints	0
$R(F_{obs})$	0.0302
$R_w(F^2)$	0.0720
S	1.065
shift/error$_{max}$	0.001
max electron density/e Å^{-3}	0.380
min electron density/e Å^{-3}	−0.271

refined as a racemic twin, volume ratio 0.4/0.6



362

CCDC number	948943
net formula	$C_{14}H_{14}Cl_4O$
M_r/g mol^{-1}	340.071
crystal size/mm	0.23 × 0.12 × 0.09
T/K	173(2)
radiation	MoKα
diffractometer	'KappaCCD'
crystal system	triclinic
space group	P1bar
a/Å	6.5349(2)
b/Å	8.8020(4)
c/Å	11.7531(5)
α/°	89.290(2)
β/°	85.351(3)
γ/°	89.283(3)
V/Å^3	673.72(5)
Z	2
calc. density/g cm^{-3}	1.67639(12)
μ/mm^{-1}	0.865
absorption correction	none
refls. measured	5617
R_{int}	0.0208
mean σ(I)/I	0.0318
θ range	3.45–27.60
observed refls.	2682
x, y (weighting scheme)	0.0296, 0.6114
hydrogen refinement	constr
refls in refinement	3112
parameters	172
restraints	0
$R(F_{obs})$	0.0326
$R_w(F^2)$	0.0820
S	1.041
shift/error$_{max}$	0.001
max electron density/e Å^{-3}	0.681
min electron density/e Å^{-3}	−0.253

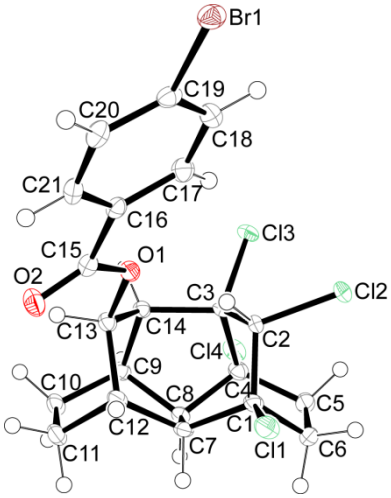


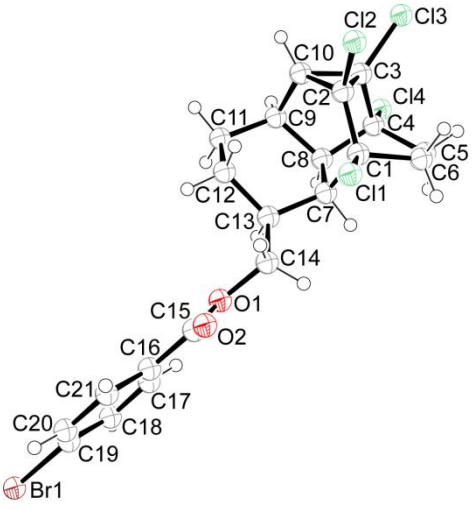
367

net formula	$C_{21}H_{19}BrCl_4O_2$
M_r/g mol^{-1}	525.089
crystal size/mm	0.168 × 0.130 × 0.102
T/K	100(2)
radiation	'Mo Kα
diffractometer	'Bruker D8Venture'
crystal system	monoclinic
space group	$P2_1/n$
a/Å	9.3536(4)
b/Å	24.7828(12)
c/Å	9.5471(5)
α/°	90
β/°	113.3625(13)
γ/°	90
V/Å^3	2031.66(17)
Z	4
calc. density/g cm^{-3}	1.71671(14)
μ/mm^{-1}	2.565
absorption correction	multi-scan
transmission factor range	0.7783–0.8621
refls. measured	41320
R_{int}	0.0355
mean σ(I)/I	0.0208
θ range	3.06–27.56
observed refls.	4138
x, y (weighting scheme)	0.0253, 1.5188
hydrogen refinement	constr
refls in refinement	4685
parameters	253
restraints	0
$R(F_{obs})$	0.0260
$R_w(F^2)$	0.0597
S	1.065
shift/error$_{max}$	0.001
max electron density/e Å^{-3}	0.471
min electron density/e Å^{-3}	−0.274

368

net formula	$C_{21}H_{19}BrCl_4O_2$
M_r/g mol^{-1}	525.089
crystal size/mm	0.103 × 0.091 × 0.014
T/K	100(2)
radiation	'Mo Kα
diffractometer	'Bruker D8Venture'
crystal system	monoclinic
space group	$P2_1/c$
a/Å	7.4572(8)
b/Å	27.474(3)
c/Å	11.5635(10)
α/°	90
β/°	118.660(5)
γ/°	90
V/Å^3	2078.9(4)
Z	4
calc. density/g cm^{-3}	1.6777(3)
μ/mm^{-1}	2.507
absorption correction	multi-scan
transmission factor range	0.6475–0.7452
refls. measured	27299
R_{int}	0.1177
mean σ(I)/I	0.0750
θ range	3.11–25.54
observed refls.	2976
x, y (weighting scheme)	0.0165, 11.3105
hydrogen refinement	constr
refls in refinement	3890
parameters	253
restraints	0
$R(F_{obs})$	0.0773
$R_w(F^2)$	0.1406
S	1.280
shift/error$_{max}$	0.001
max electron density/e Å^{-3}	0.831
min electron density/e Å^{-3}	−0.626

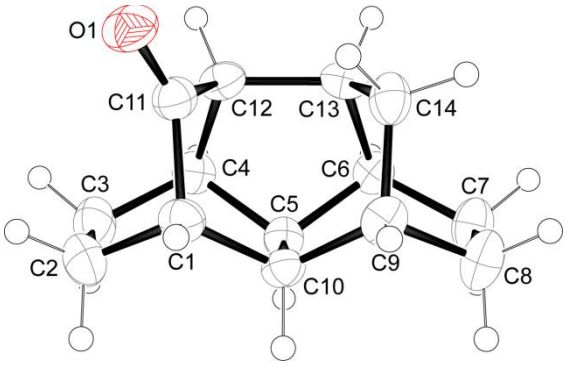




371

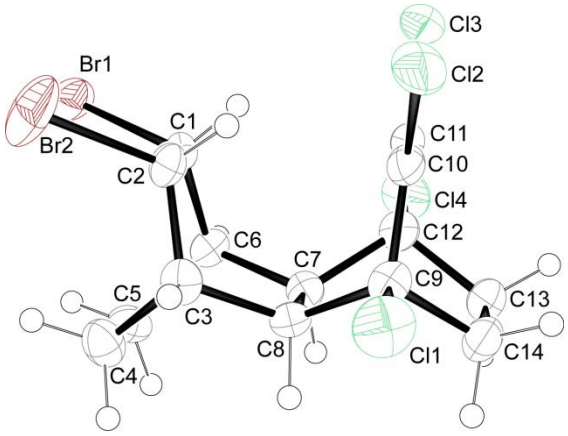
CCDC number	948941
net formula	$C_{14}H_{18}O$
M_r/g mol^{-1}	202.292
crystal size/mm	0.24 × 0.12 × 0.03
T/K	173(2)
radiation	MoKα
diffractometer	'KappaCCD'
crystal system	triclinic
space group	P1bar
a/Å	6.2093(4)
b/Å	8.3668(5)
c/Å	11.1450(5)
α/°	74.540(3)
β/°	89.252(3)
γ/°	68.175(3)
V/Å^3	515.66(5)
Z	2
calc. density/g cm^{-3}	1.30287(13)
μ/mm^{-1}	0.079
absorption correction	none
refls. measured	4338
R_{int}	0.0410
mean σ(I)/I	0.0552
θ range	3.55–27.55
observed refls.	1540
x, y (weighting scheme)	0.0579, 0.0876
hydrogen refinement	constr
refls in refinement	2364
parameters	200
restraints	0
$R(F_{obs})$	0.0518
$R_w(F^2)$	0.1385
S	1.036
shift/error$_{max}$	0.001
max electron density/e Å^{-3}	0.178
min electron density/e Å^{-3}	−0.161

O11, C11, C12, C13 and C14 are disordered over four sites with sof 0.39, 0.25, 0.28 and 0.08 resp., split model applied.



374

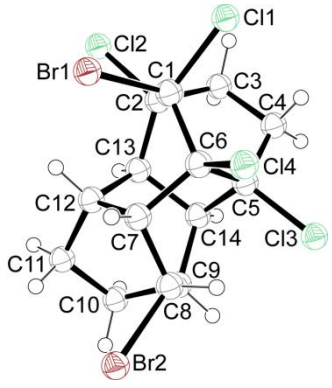
CCDC number	948944
net formula	$C_{14}H_{14}Br_2Cl_4$
M_r/g mol^{-1}	483.880
crystal size/mm	0.03 × 0.03 × 0.02
T/K	173(2)
radiation	MoKα
diffractometer	'KappaCCD'
crystal system	monoclinic
space group	$P2_1/c$
a/Å	14.7642(7)
b/Å	7.4391(3)
c/Å	14.5856(6)
α/°	90
β/°	91.061(2)
γ/°	90
V/Å^3	1601.70(12)
Z	4
calc. density/g cm^{-3}	2.00665(15)
μ/mm^{-1}	5.714
absorption correction	none
refls. measured	9823
R_{int}	0.0867
mean σ(I)/I	0.0662
θ range	3.14–25.35
observed refls.	2061
x, y (weighting scheme)	0.0395, 0.0737
hydrogen refinement	constr
refls in refinement	2911
parameters	181
restraints	0
$R(F_{obs})$	0.0366
$R_w(F^2)$	0.0903
S	1.028
shift/error$_{max}$	0.001
max electron density/e Å^{-3}	0.827
min electron density/e Å^{-3}	−0.722



376

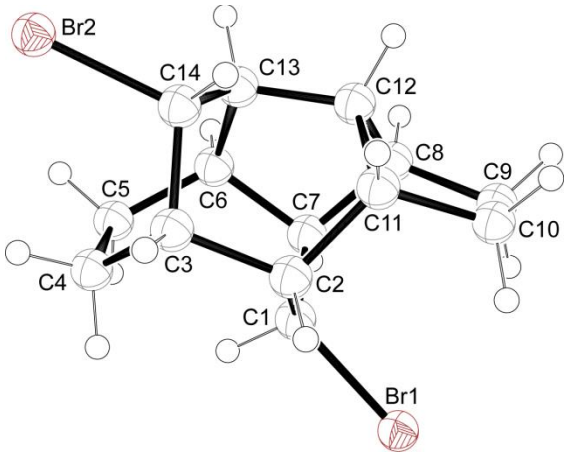
CCDC number	948945
net formula	$C_{14}H_{14}Br_2Cl_4$
M_r/g mol^{-1}	483.880
crystal size/mm	0.16 × 0.10 × 0.06
T/K	173(2)
radiation	MoKα
diffractometer	'Oxford XCalibur'
crystal system	monoclinic
space group	$P2_1/c$
a/Å	8.5158(3)
b/Å	12.1809(5)
c/Å	14.7928(5)
α/°	90
β/°	98.852(3)
γ/°	90
V/Å^3	1516.18(10)
Z	4
calc. density/g cm^{-3}	2.11983(14)
μ/mm^{-1}	6.037
absorption correction	'multi-scan'
transmission factor range	0.54047–1.00000
refls. measured	8102
R_{int}	0.0410
mean σ(I)/I	0.0415
θ range	4.24–26.36
observed refls.	2662
x, y (weighting scheme)	0.0771, 0.4065
hydrogen refinement	constr
refls in refinement	3084
parameters	182
restraints	0
$R(F_{obs})$	0.0424
$R_w(F^2)$	0.1162
S	1.025
shift/error$_{max}$	0.001
max electron density/e Å^{-3}	1.090
min electron density/e Å^{-3}	−1.433

Br1 and Cl1 bound to C1 are disordered: the site of Br1 is occupied by Cl11 as well and the site of Cl1 is occupied by Br11, sof ratio 0.7/0.3.



380

CCDC number	948947
net formula	$C_{14}H_{18}Br_2$
M_r/g mol^{-1}	346.101
crystal size/mm	0.167 × 0.097 × 0.090
T/K	100(2)
radiation	'Mo Kα
diffractometer	'Bruker D8Venture'
crystal system	monoclinic
space group	$P2_1/c$
a/Å	14.3718(4)
b/Å	6.4978(2)
c/Å	12.7356(4)
α/°	90
β/°	94.731(2)
γ/°	90
V/Å^3	1185.26(6)
Z	4
calc. density/g cm^{-3}	1.93956(10)
μ/mm^{-1}	6.808
absorption correction	multi-scan
transmission factor range	0.6207–0.7457
refls. measured	22884
R_{int}	0.0451
mean σ(I)/I	0.0278
θ range	3.21–28.41
observed refls.	2534
x, y (weighting scheme)	0.0248, 0.6269
hydrogen refinement	constr
refls in refinement	2948
parameters	145
restraints	0
$R(F_{obs})$	0.0233
$R_w(F^2)$	0.0520
S	1.054
shift/error$_{max}$	0.001
max electron density/e Å^{-3}	0.508
min electron density/e Å^{-3}	−0.342

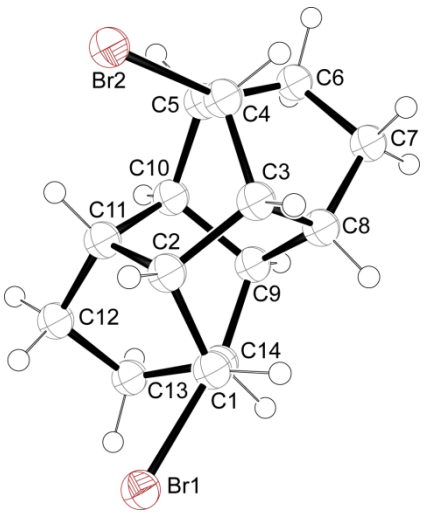


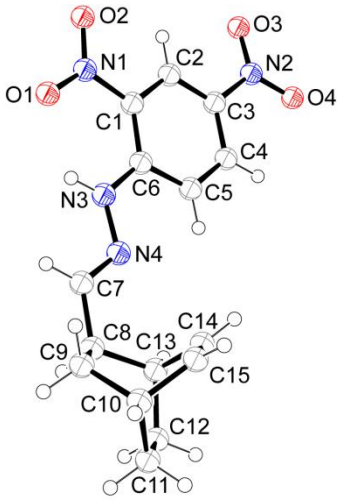
382

CCDC number	948946
net formula	$C_{14}H_{18}Br_2$
M_r/g mol^{-1}	346.101
crystal size/mm	0.26 × 0.19 × 0.04
T/K	173(2)
radiation	MoKα
diffractometer	'Oxford XCalibur'
crystal system	monoclinic
space group	$P2_1/c$
a/Å	13.0330(10)
b/Å	7.7467(6)
c/Å	12.4282(9)
α/°	90
β/°	101.998(7)
γ/°	90
V/Å^3	1227.37(16)
Z	4
calc. density/g cm^{-3}	1.8730(2)
μ/mm^{-1}	6.574
absorption correction	'multi-scan'
transmission factor range	0.41499–1.00000
refls. measured	4608
R_{int}	0.0303
mean σ(I)/I	0.0516
θ range	4.21–28.84
observed refls.	2166
x, y (weighting scheme)	0.0453, 0.2889
hydrogen refinement	constr
refls in refinement	2708
parameters	145
restraints	0
$R(F_{obs})$	0.0390
$R_w(F^2)$	0.1006
S	1.051
shift/error$_{max}$	0.001
max electron density/e Å^{-3}	0.878
min electron density/e Å^{-3}	−0.977

417

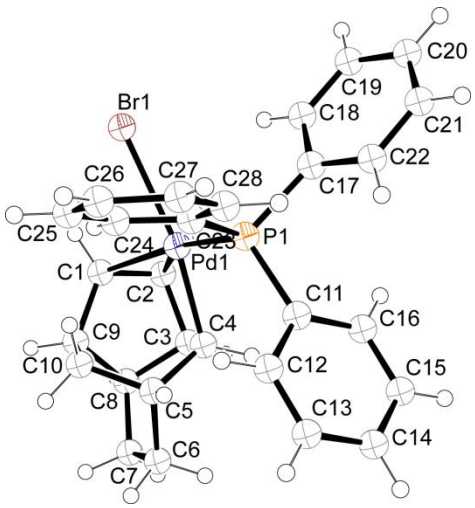
net formula	$C_{15}H_{16}N_4O_4$
M_r/g mol^{-1}	316.317
crystal size/mm	0.20 × 0.05 × 0.03
T/K	200(2)
radiation	MoKα
diffractometer	'Oxford XCalibur'
crystal system	monoclinic
space group	$P2_1/c$
a/Å	14.3246(9)
b/Å	7.2254(4)
c/Å	14.0554(8)
α/°	90
β/°	97.528(5)
γ/°	90
V/Å^3	1442.21(15)
Z	4
calc. density/g cm^{-3}	1.457
μ/mm^{-1}	0.108
absorption correction	none
refls. measured	18393
R_{int}	0.0676
mean σ(I)/I	0.0813
θ range	4.18–25.99
observed refls.	1409
hydrogen refinement	mixed
refls in refinement	2817
parameters	199
restraints	0
$R(F_{obs})$	0.0399
$R_w(F^2)$	0.0747
S	0.796
shift/error$_{max}$	0.001
max electron density/e Å^{-3}	0.169
min electron density/e Å^{-3}	−0.173





420

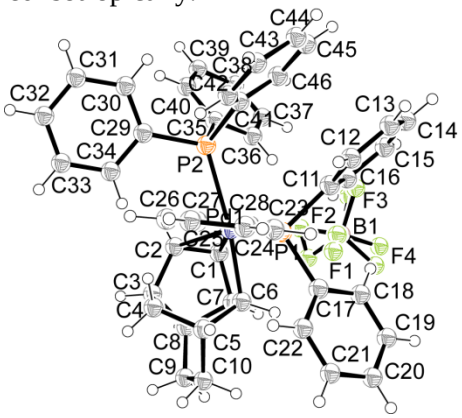
CCDC number	1000370
net formula	$C_{28}H_{28}BrPPd$
M_r/g mol^{-1}	581.82
crystal size/mm	0.32 × 0.28 × 0.05
T/K	173(2)
radiation	MoKα
diffractometer	'Oxford XCalibur'
crystal system	monoclinic
space group	$P2_1/c$
a/Å	9.5062(3)
b/Å	19.6014(6)
c/Å	12.7805(5)
α/°	90
β/°	103.203(4)
γ/°	90
V/Å^3	2318.50(14)
Z	4
calc. density/g cm^{-3}	1.66685(10)
μ/mm^{-1}	2.607
absorption correction	'multi-scan'
transmission factor range	0.90792–1.00000
refls. measured	10297
R_{int}	0.0299
mean σ(I)/I	0.0580
θ range	4.34–26.34
observed refls.	3400
x, y (weighting scheme)	0.0221, 0
hydrogen refinement	constr
refls in refinement	4691
parameters	280
restraints	0
$R(F_{obs})$	0.0282
$R_w(F^2)$	0.0551
S	0.886
shift/error$_{max}$	0.001
max electron density/e Å^{-3}	0.631
min electron density/e Å^{-3}	−0.900



421

CCDC number	1000372
net formula	$C_{46}H_{43}BF_4P_2Pd$
M_r/g mol^{-1}	851.01
crystal size/mm	0.25 × 0.12 × 0.09
T/K	200(2)
radiation	MoKα
diffractometer	'KappaCCD'
crystal system	monoclinic
space group	$P2_1/n$
a/Å	10.13000(10)
b/Å	18.4054(2)
c/Å	21.4910(3)
α/°	90
β/°	102.2909(7)
γ/°	90
V/Å^3	3915.08(8)
Z	4
calc. density/g cm^{-3}	1.44380(3)
μ/mm^{-1}	0.608
absorption correction	multi-scan
transmission factor range	0.7928–0.9144
refls. measured	66313
R_{int}	0.0486
mean σ(I)/I	0.0325
θ range	3.19–27.54
observed refls.	7300
x, y (weighting scheme)	0.0554, 5.0285
hydrogen refinement	constr
refls in refinement	8985
parameters	484
restraints	0
$R(F_{obs})$	0.0412
$R_w(F^2)$	0.1123
S	1.036
shift/error$_{max}$	0.002
max electron density/e Å^{-3}	0.954
min electron density/e Å^{-3}	−0.910

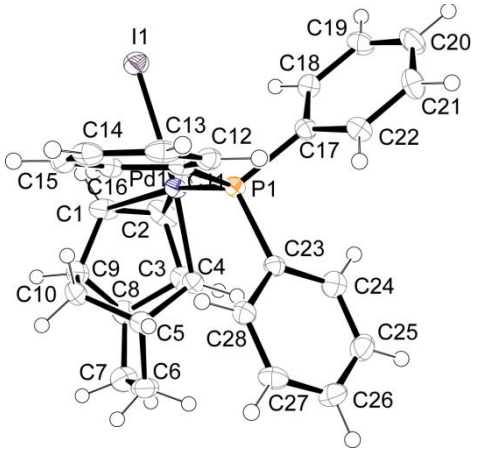
BF_4^- disordered, refined using split model, sof 0.48/0.52, less occupied disordered atoms were refined isotropically.



424

CCDC number	1000371
net formula	$C_{28}H_{28}IPPd$
M_r/g mol^{-1}	628.82
crystal size/mm	0.24 × 0.20 × 0.16
T/K	173(2)
radiation	MoKα
diffractometer	'Oxford XCalibur'
crystal system	triclinic
space group	P1bar
a/Å	10.0947(6)
b/Å	10.7380(5)
c/Å	12.1614(5)
α/°	102.574(4)
β/°	108.942(5)
γ/°	98.328(4)
V/Å^3	1183.34(12)
Z	2
calc. density/g cm^{-3}	1.76483(15)
μ/mm^{-1}	2.170
absorption correction	'multi-scan'
transmission factor range	0.97763–1.00000
refls. measured	8291
R_{int}	0.0255
mean σ(I)/I	0.0525
θ range	4.31–26.33
observed refls.	3620
x, y (weighting scheme)	0.0207, 0
hydrogen refinement	mixed
refls in refinement	4787
parameters	286
restraints	0
$R(F_{obs})$	0.0277
$R_w(F^2)$	0.0558
S	0.933
shift/error$_{max}$	0.003
max electron density/e Å^{-3}	0.758
min electron density/e Å^{-3}	−0.648

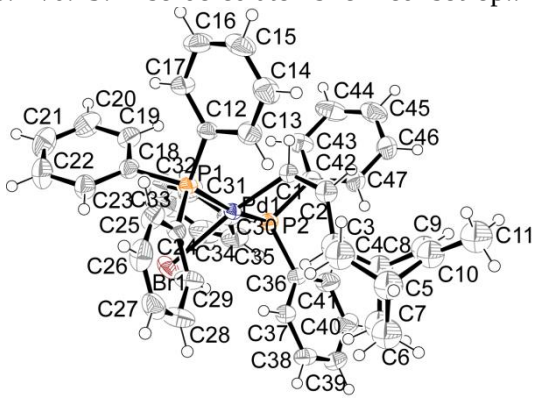
H atoms bound to C atoms of the Pd-linked double bond: refxyz with U(H) = 1.2 U(C), all other H: constr.



448

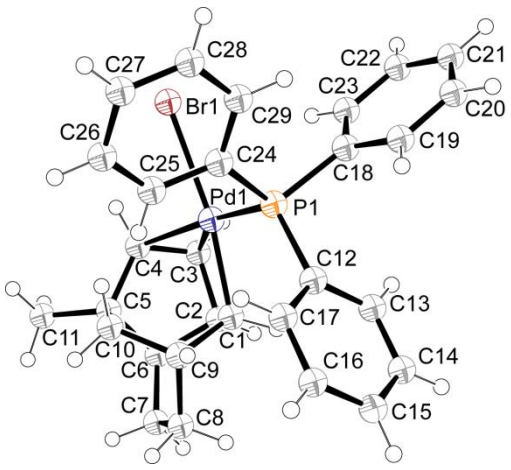
CCDC number	1000374
Net formula	$C_{51.59}H_{53.82}BrO_{0.71}P_2Pd$
M_r/g mol^{-1}	933.37
crystal size/mm	0.25 × 0.14 × 0.06
T/K	123(2)
radiation	MoKα
diffractometer	'KappaCCD'
crystal system	triclinic
space group	P1bar
a/Å	9.7334(2)
b/Å	15.2486(2)
c/Å	16.0612(3)
α/°	87.8046(10)
β/°	80.8502(11)
γ/°	72.6476(10)
V/Å^3	2246.27(7)
Z	2
calc. density/g cm^{-3}	1.38007(4)
μ/mm^{-1}	1.409
absorption correction	multi-scan
transmission factor range	0.7544–0.8470
refls. measured	49441
R_{int}	0.0406
mean σ(I)/I	0.0388
θ range	3.15–27.46
observed refls.	8444
x, y (weighting scheme)	0.0418, 4.4726
hydrogen refinement	constr
refls in refinement	10234
parameters	470
restraints	25
$R(F_{obs})$	0.0440
$R_w(F^2)$	0.1094
S	1.020
shift/error$_{max}$	0.001
max electron density/e Å^{-3}	1.258
min electron density/e Å^{-3}	−1.026

organic ligand disordered, split model applied, sof 0.72/0.28. Et_2O and C_6H_6 disordered. sof 0.71/0.29. Disordered atoms refined isotrop..



450

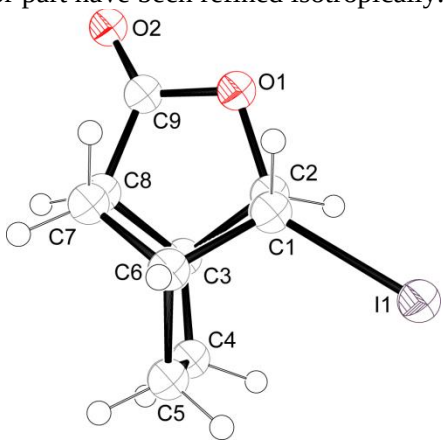
CCDC number	1000373
net formula	$C_{29}H_{30}BrPPd$
M_r/g mol^{-1}	595.85
crystal size/mm	0.30 × 0.27 × 0.23
T/K	173(2)
radiation	MoKα
diffractometer	'Oxford XCalibur'
crystal system	monoclinic
space group	$P2_1/c$
a/Å	13.3791(3)
b/Å	9.9376(2)
c/Å	19.0528(5)
α/°	90
β/°	97.985(2)
γ/°	90
V/Å^3	2508.63(10)
Z	4
calc. density/g cm^{-3}	1.57766(6)
μ/mm^{-1}	2.411
absorption correction	'multi-scan'
transmission factor range	0.93132–1.00000
refls. measured	18759
R_{int}	0.0273
mean σ(I)/I	0.0362
θ range	4.24–26.35
observed refls.	4027
x, y (weighting scheme)	0.0229, 0
hydrogen refinement	constr
refls in refinement	5085
parameters	290
restraints	0
$R(F_{obs})$	0.0208
$R_w(F^2)$	0.0446
S	0.920
shift/error$_{max}$	0.003
max electron density/e Å^{-3}	0.387
min electron density/e Å^{-3}	−0.407



474

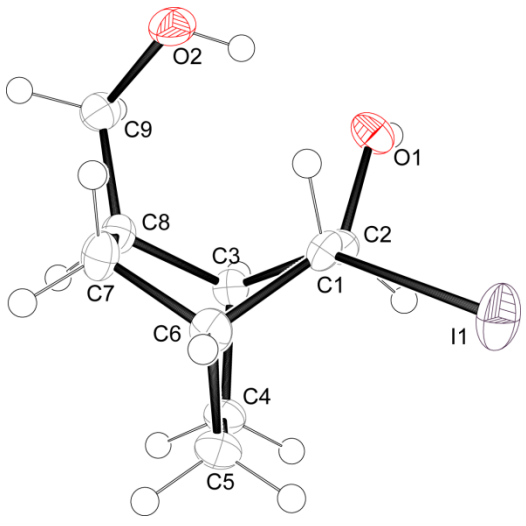
net formula	$C_9H_{11}IO_2$
M_r/g mol^{-1}	278.087
crystal size/mm	0.16 × 0.11 × 0.07
T/K	173(2)
radiation	MoKα
diffractometer	'KappaCCD'
crystal system	orthorhombic
space group	*Pbca*
a/Å	11.6393(1)
b/Å	11.7748(1)
c/Å	26.6489(3)
α/°	90
β/°	90
γ/°	90
V/Å^3	3652.24(6)
Z	16
calc. density/g cm^{-3}	2.02300(3)
μ/mm^{-1}	3.463
absorption correction	multi-scan
transmission factor range	0.5915–0.7142
refls. measured	57539
R_{int}	0.0326
mean σ(I)/I	0.0163
θ range	3.36–27.50
observed refls.	3577
x, y (weighting scheme)	0.0202, 13.1544
hydrogen refinement	constr
refls in refinement	4183
parameters	234
restraints	0
$R(F_{obs})$	0.0291
$R_w(F^2)$	0.0658
S	1.017
shift/error$_{max}$	0.001
max electron density/e Å^{-3}	0.957
min electron density/e Å^{-3}	−0.928

One of the two symmetrically independent molecules is partly disordered, split model applied, sof 0.71/0.29, disordered atoms of the minor part have been refined isotropically.



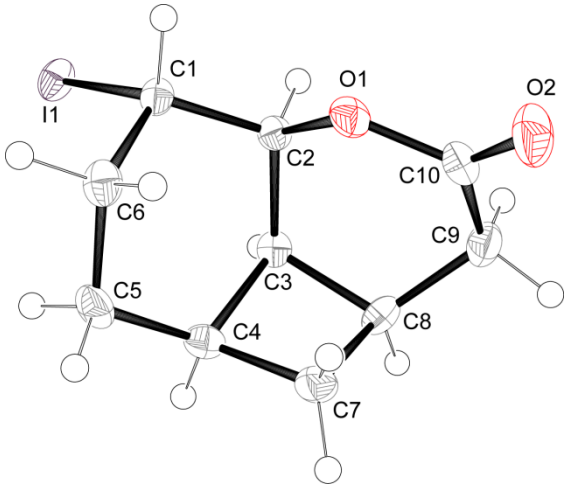
476

net formula	$C_9H_{15}IO_2$
M_r/g mol^{-1}	282.119
crystal size/mm	0.33 × 0.17 × 0.12
T/K	173(2)
radiation	MoKα
diffractometer	'Oxford XCalibur'
crystal system	monoclinic
space group	$P2_1/c$
a/Å	11.6297(7)
b/Å	6.3581(2)
c/Å	13.5837(6)
α/°	90
β/°	103.381(5)
γ/°	90
V/Å^3	977.15(8)
Z	4
calc. density/g cm^{-3}	1.91772(16)
μ/mm^{-1}	3.237
absorption correction	'multi-scan'
transmission factor range	0.74640–1.00000
refls. measured	7570
R_{int}	0.0245
mean σ(I)/I	0.0242
θ range	4.14–26.35
observed refls.	1665
x, y (weighting scheme)	0.0247, 0
hydrogen refinement	constr
refls in refinement	1979
parameters	111
restraints	0
$R(F_{obs})$	0.0197
$R_w(F^2)$	0.0456
S	0.990
shift/error$_{max}$	0.001
max electron density/e Å^{-3}	0.431
min electron density/e Å^{-3}	−0.495



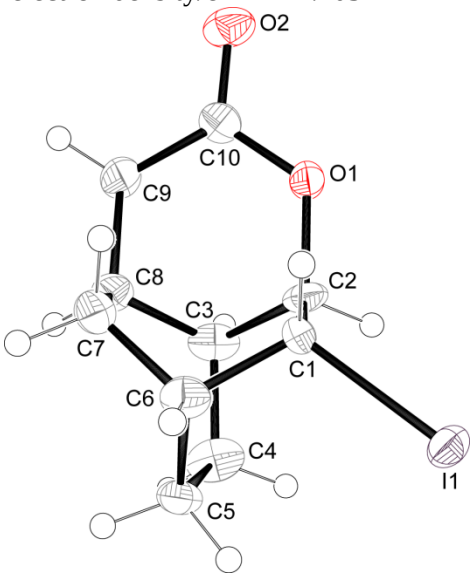
481

CCDC number	1000375
net formula	$C_{10}H_{13}IO_2$
M_r/g mol^{-1}	292.113
crystal size/mm	0.40 × 0.30 × 0.25
T/K	173(2)
radiation	MoKα
diffractometer	'Oxford XCalibur'
crystal system	orthorhombic
space group	$Pna2_1$
a/Å	10.1335(3)
b/Å	6.3717(3)
c/Å	31.1401(10)
α/°	90
β/°	90
γ/°	90
V/Å^3	2010.64(13)
Z	8
calc. density/g cm^{-3}	1.93002(12)
μ/mm^{-1}	3.150
absorption correction	'multi-scan'
transmission factor range	0.84938–1.00000
refls. measured	15806
R_{int}	0.0264
mean σ(I)/I	0.0278
θ range	4.23–29.99
observed refls.	4453
x, y (weighting scheme)	0.0185, 2.9678
hydrogen refinement	constr
Flack parameter	0.00(2)
refls in refinement	4807
parameters	235
restraints	1
$R(F_{obs})$	0.0269
$R_w(F^2)$	0.0588
S	1.085
shift/error$_{max}$	0.001
max electron density/e Å^{-3}	0.955
min electron density/e Å^{-3}	−1.236



249

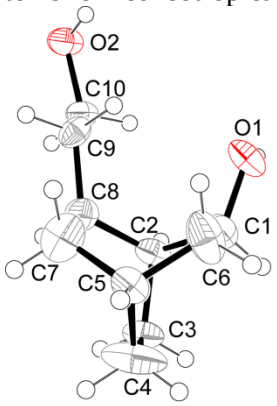
CCDC number	1000376
net formula	$C_{10}H_{13}IO_2$
M_r/g mol^{-1}	292.113
crystal size/mm	0.18 × 0.06 × 0.03
T/K	173(2)
radiation	MoKα
diffractometer	'Oxford XCalibur'
crystal system	monoclinic
space group	$P2_1/c$
a/Å	6.6232(5)
b/Å	9.2703(7)
c/Å	16.0938(16)
α/°	90
β/°	91.834(8)
γ/°	90
V/Å^3	987.64(14)
Z	4
calc. density/g cm^{-3}	1.9646(3)
μ/mm^{-1}	3.207
absorption correction	'multi-scan'
transmission factor range	0.39731–1.00000
refls. measured	5545
R_{int}	0.0446
mean σ(I)/I	0.0476
θ range	4.39–26.36
observed refls.	1752
x, y (weighting scheme)	0.0382, 4.9934
hydrogen refinement	constr
refls in refinement	2011
parameters	118
restraints	0
$R(F_{obs})$	0.0467
$R_w(F^2)$	0.1138
S	1.177
shift/error$_{max}$	0.001
max electron density/e Å^{-3}	2.203
min electron density/e Å^{-3}	−1.205



251

CCDC number	1000377
net formula	$C_{10}H_{18}O_2$
M_r/g mol^{-1}	170.249
crystal size/mm	0.2504 × 0.1855 × 0.1735
T/K	173(2)
radiation	MoKα
diffractometer	'Oxford XCalibur'
crystal system	monoclinic
space group	$P2_1/c$
a/Å	12.7135(12)
b/Å	8.5955(8)
c/Å	8.7809(7)
α/°	90
β/°	101.702(8)
γ/°	90
V/Å^3	939.62(15)
Z	4
calc. density/g cm^{-3}	1.20350(19)
μ/mm^{-1}	0.081
absorption correction	'multi-scan'
transmission factor range	0.84909–1.00000
refls. measured	3173
R_{int}	0.0209
mean σ(I)/I	0.0431
θ range	4.34–26.37
observed refls.	1387
x, y (weighting scheme)	0.0965, 0.8658
hydrogen refinement	constr
refls in refinement	1907
parameters	120
restraints	1
$R(F_{obs})$	0.0759
$R_w(F^2)$	0.2189
S	1.059
shift/error$_{max}$	0.001
max electron density/e Å^{-3}	0.543
min electron density/e Å^{-3}	−0.352

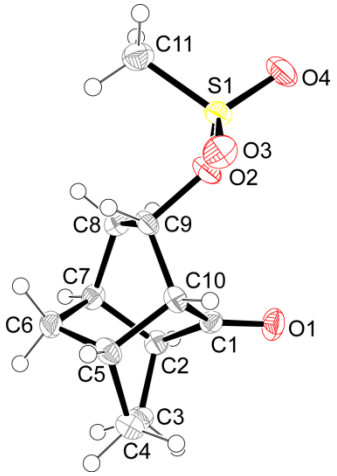
Side chain partly disordered, split model applied, sof ratio 0.84/0.16, less occupied disordered atoms refined isotropically.



485

CCDC number	1000378
net formula	$C_{11}H_{16}O_4S$
M_r/g mol^{-1}	244.308
crystal size/mm	0.12 × 0.08 × 0.03
T/K	173(2)
radiation	MoKα
diffractometer	'KappaCCD'
crystal system	orthorhombic
space group	$P2_12_12_1$
a/Å	6.4001(2)
b/Å	8.8476(2)
c/Å	19.4784(5)
α/°	90
β/°	90
γ/°	90
V/Å^3	1102.97(5)
Z	4
calc. density/g cm^{-3}	1.47126(7)
μ/mm^{-1}	0.290
absorption correction	none
refls. measured	8201
R_{int}	0.0378
mean σ(I)/I	0.0379
θ range	3.35–27.49
observed refls.	2180
x, y (weighting scheme)	0.0349, 0.2957
hydrogen refinement	constr
Flack parameter	0.22(9)
refls in refinement	2531
parameters	147
restraints	0
$R(F_{obs})$	0.0345
$R_w(F^2)$	0.0800
S	1.062
shift/error$_{max}$	0.001
max electron density/e Å^{-3}	0.171
min electron density/e Å^{-3}	−0.384

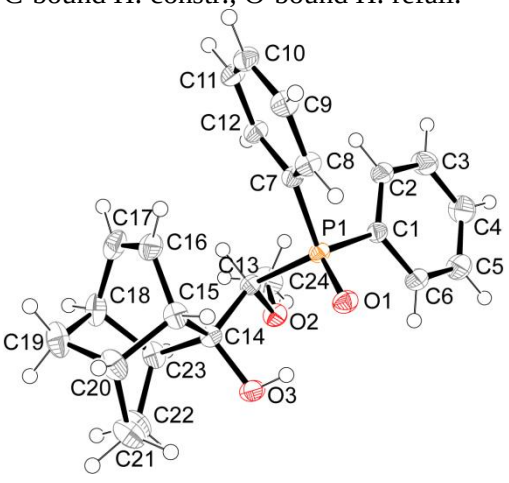
Refined as racemic twin, volume ratio 0.22/0.78.



490

CCDC number	1000379
net formula	$C_{24}H_{27}O_3P$
M_r/g mol^{-1}	394.443
crystal size/mm	0.40 × 0.30 × 0.17
T/K	173(2)
radiation	MoKα
diffractometer	'Oxford XCalibur'
crystal system	triclinic
space group	P1bar
a/Å	7.2398(4)
b/Å	9.5416(4)
c/Å	14.6831(9)
α/°	90.040(4)
β/°	81.463(5)
γ/°	85.164(4)
V/Å^3	999.40(9)
Z	2
calc. density/g cm^{-3}	1.31078(12)
μ/mm^{-1}	0.160
absorption correction	'multi-scan'
transmission factor range	0.96932–1.00000
refls. measured	8998
R_{int}	0.0169
mean σ(I)/I	0.0345
θ range	4.17–30.50
observed refls.	5051
x, y (weighting scheme)	0.0485, 0.2722
hydrogen refinement	mixed
refls in refinement	6024
parameters	258
restraints	0
$R(F_{obs})$	0.0401
$R_w(F^2)$	0.1090
S	1.046
shift/error$_{max}$	0.001
max electron density/e Å^{-3}	0.402
min electron density/e Å^{-3}	−0.257

C-bound H: constr., O-bound H: refall.

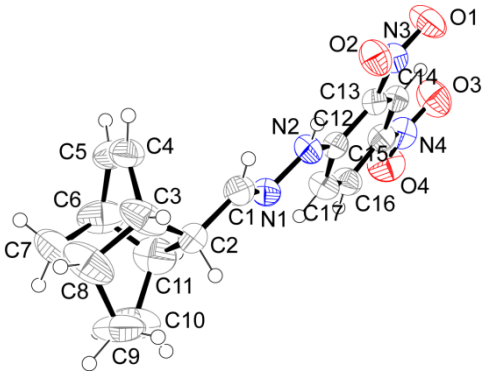


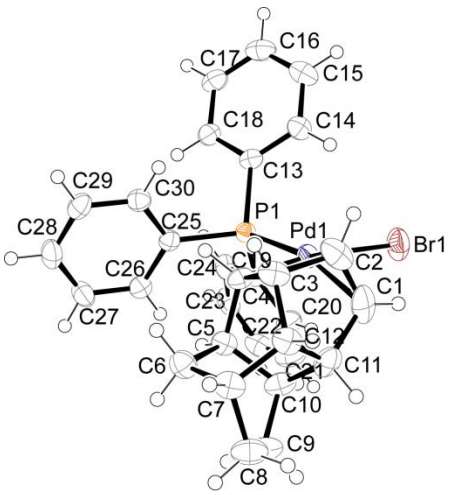
493

CCDC number	1000380
net formula	$C_{17}H_{18}N_4O_4$
M_r/g mol^{-1}	342.349
crystal size/mm	0.34 × 0.29 × 0.07
T/K	200(2)
radiation	MoKα
diffractometer	'KappaCCD'
crystal system	monoclinic
space group	$P2_1/c$
a/Å	10.5480(5)
b/Å	20.8588(10)
c/Å	7.6700(3)
α/°	90
β/°	110.904(2)
γ/°	90
V/Å^3	1576.47(12)
Z	4
calc. density/g cm^{-3}	1.44244(11)
μ/mm^{-1}	0.105
absorption correction	none
refls. measured	10564
R_{int}	0.0523
mean σ(I)/I	0.0407
θ range	3.45–25.46
observed refls.	1974
x, y (weighting scheme)	0.1190, 3.9357
hydrogen refinement	constr
refls in refinement	2887
parameters	226
restraints	0
$R(F_{obs})$	0.1035
$R_w(F^2)$	0.2965
S	1.058
shift/error$_{max}$	0.001
max electron density/e Å^{-3}	1.127
min electron density/e Å^{-3}	−0.413

512

CCDC number	1000381
net formula	$C_{30}H_{30}BrPPd$
M_r/g mol^{-1}	607.86
crystal size/mm	0.22 × 0.14 × 0.11
T/K	200(2)
radiation	MoKα
diffractometer	'KappaCCD'
crystal system	monoclinic
space group	$P2_1/c$
a/Å	10.0125(2)
b/Å	19.3538(4)
c/Å	13.1438(2)
α/°	90
β/°	105.8240(10)
γ/°	90
V/Å^3	2450.48(8)
Z	4
calc. density/g cm^{-3}	1.64765(5)
μ/mm^{-1}	2.470
absorption correction	multi-scan
transmission factor range	0.6198–0.7142
refls. measured	40313
R_{int}	0.0689
mean σ(I)/I	0.0427
θ range	3.17–27.80
observed refls.	4597
x, y (weighting scheme)	0.0285, 1.7410
hydrogen refinement	constr
refls in refinement	5698
parameters	298
restraints	0
$R(F_{obs})$	0.0321
$R_w(F^2)$	0.0766
S	1.037
shift/error$_{max}$	0.001
max electron density/e Å^{-3}	0.596
min electron density/e Å^{-3}	−0.403



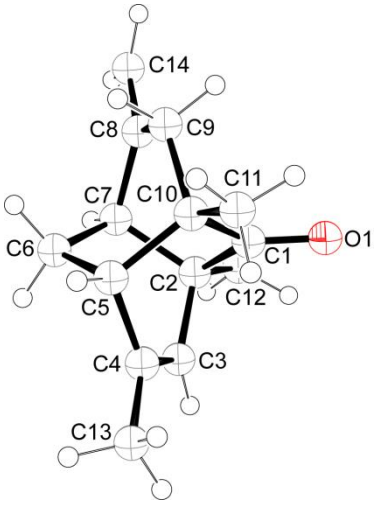


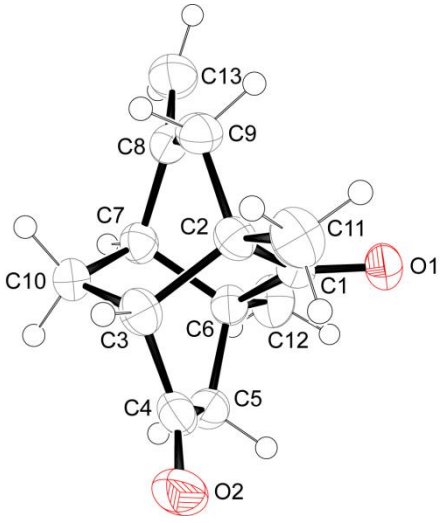
558

net formula	$C_{14}H_{18}O$
M_r/g mol^{-1}	202.292
crystal size/mm	0.26 × 0.24 × 0.21
T/K	173(2)
radiation	MoKα
diffractometer	'KappaCCD'
crystal system	monoclinic
space group	*Cc*
a/Å	8.2827(2)
b/Å	11.7902(3)
c/Å	11.9036(3)
α/°	90
β/°	96.7285(18)
γ/°	90
V/Å^3	1154.44(5)
Z	4
calc. density/g cm^{-3}	1.16392(5)
μ/mm^{-1}	0.071
absorption correction	none
refls. measured	4600
R_{int}	0.0157
mean σ(I)/I	0.0240
θ range	3.46–27.48
observed refls.	2270
x, y (weighting scheme)	0.0621, 0.5474
hydrogen refinement	constr
Flack parameter	0(4)
refls in refinement	2558
parameters	139
restraints	2
$R(F_{obs})$	0.0448
$R_w(F^2)$	0.1217
S	1.059
shift/error$_{max}$	0.001
max electron density/e Å^{-3}	0.245
min electron density/e Å^{-3}	−0.161

563

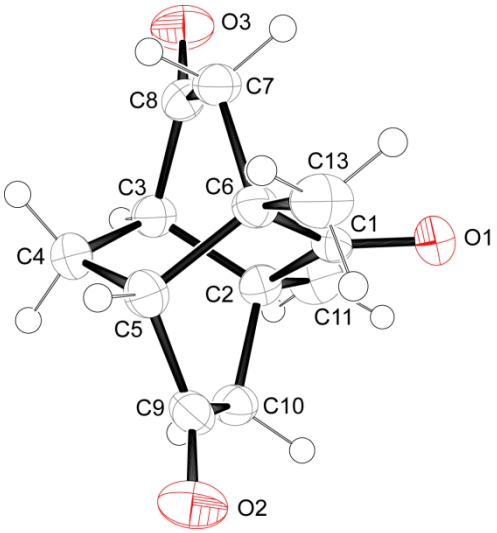
net formula	$C_{13}H_{16}O_2$
M_r/g mol^{-1}	204.265
crystal size/mm	0.33 × 0.17 × 0.08
T/K	173(2)
radiation	MoKα
diffractometer	'KappaCCD'
crystal system	monoclinic
space group	$P2_1/c$
a/Å	12.4334(7)
b/Å	8.1284(5)
c/Å	11.3242(5)
α/°	90
β/°	106.735(4)
γ/°	90
V/Å^3	1095.99(10)
Z	4
calc. density/g cm^{-3}	1.23795(11)
μ/mm^{-1}	0.082
absorption correction	none
refls. measured	7122
R_{int}	0.0327
mean σ(I)/I	0.0271
θ range	3.30–25.38
observed refls.	1693
x, y (weighting scheme)	0.0358, 0.4853
hydrogen refinement	constr
refls in refinement	1984
parameters	138
restraints	0
$R(F_{obs})$	0.0428
$R_w(F^2)$	0.1059
S	1.086
shift/error$_{max}$	0.001
max electron density/e Å^{-3}	0.166
min electron density/e Å^{-3}	−0.150





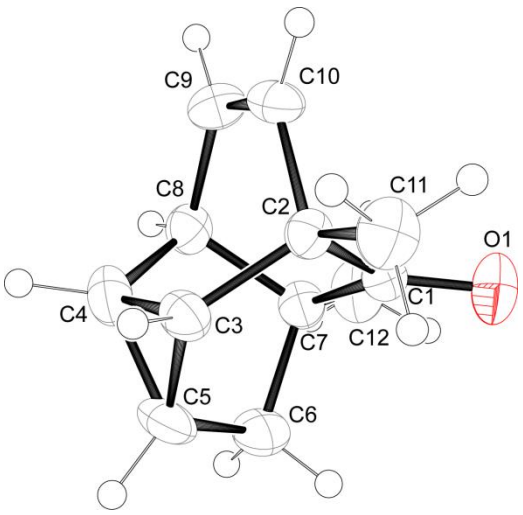
564

net formula	$C_{12}H_{14}O_3$
M_r/g mol^{-1}	206.238
crystal size/mm	0.25 × 0.13 × 0.10
T/K	173(2)
radiation	MoKα
diffractometer	'KappaCCD'
crystal system	monoclinic
space group	$P2_1/c$
a/Å	7.7312(3)
b/Å	11.2398(4)
c/Å	11.9728(4)
α/°	90
β/°	99.529(2)
γ/°	90
V/Å^3	1026.05(6)
Z	4
calc. density/g cm^{-3}	1.33510(8)
μ/mm^{-1}	0.095
absorption correction	none
refls. measured	6769
R_{int}	0.0308
mean σ(I)/I	0.0267
θ range	3.86–25.37
observed refls.	1548
x, y (weighting scheme)	0.0432, 0.3912
hydrogen refinement	constr
refls in refinement	1877
parameters	138
restraints	0
$R(F_{obs})$	0.0382
$R_w(F^2)$	0.0984
S	1.029
shift/error$_{max}$	0.001
max electron density/e Å^{-3}	0.209
min electron density/e Å^{-3}	−0.165



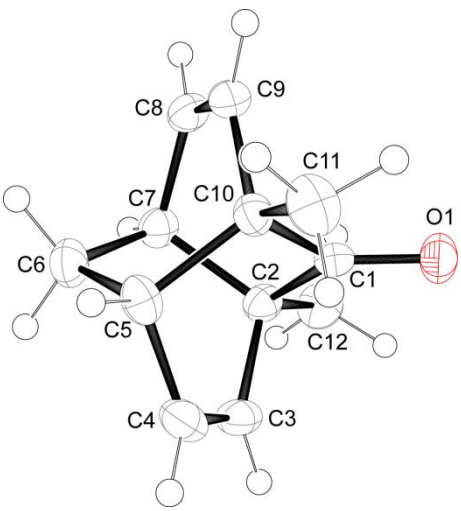
567

CCDC number	1000383
net formula	$C_{12}H_{14}O$
M_r/g mol^{-1}	174.239
crystal size/mm	0.43 × 0.37 × 0.12
T/K	173(2)
radiation	MoKα
diffractometer	'Oxford XCalibur'
crystal system	monoclinic
space group	$P2_1/n$
a/Å	6.7003(12)
b/Å	12.024(2)
c/Å	11.8106(18)
α/°	90
β/°	99.127(17)
γ/°	90
V/Å^3	939.5(3)
Z	4
calc. density/g cm^{-3}	1.2319(4)
μ/mm^{-1}	0.076
absorption correction	'multi-scan'
transmission factor range	0.40299–1.00000
refls. measured	3251
R_{int}	0.0270
mean σ(I)/I	0.0455
θ range	4.58–26.37
observed refls.	1469
x, y (weighting scheme)	0.0934, 0.1853
hydrogen refinement	constr
refls in refinement	1897
parameters	120
restraints	0
$R(F_{obs})$	0.0593
$R_w(F^2)$	0.1742
S	1.055
shift/error$_{max}$	0.001
max electron density/e Å^{-3}	0.373
min electron density/e Å^{-3}	−0.216



569

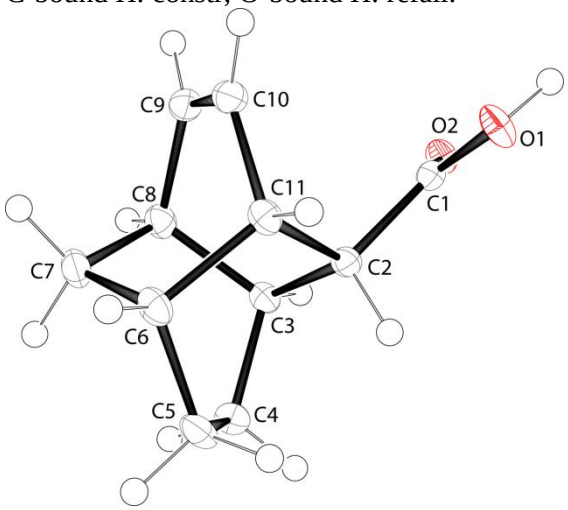
CCDC number	1000382
net formula	$C_{12}H_{14}O$
M_r/g mol^{-1}	174.239
crystal size/mm	0.25 × 0.12 × 0.05
T/K	173(2)
radiation	MoKα
diffractometer	'Oxford XCalibur'
crystal system	monoclinic
space group	$P2_1/c$
a/Å	7.1854(8)
b/Å	8.3619(10)
c/Å	15.4571(19)
α/°	90
β/°	90.185(11)
γ/°	90
V/Å^3	928.71(19)
Z	4
calc. density/g cm^{-3}	1.2462(3)
μ/mm^{-1}	0.077
absorption correction	'multi-scan'
transmission factor range	0.93518–1.00000
refls. measured	3152
R_{int}	0.0337
mean σ(I)/I	0.0537
θ range	4.57–26.37
observed refls.	1394
x, y (weighting scheme)	0.0552, 0.1579
hydrogen refinement	constr
refls in refinement	1877
parameters	120
restraints	0
$R(F_{obs})$	0.0472
$R_w(F^2)$	0.1278
S	1.047
shift/error$_{max}$	0.001
max electron density/e Å^{-3}	0.309
min electron density/e Å^{-3}	−0.252



597

net formula	$C_{11}H_{14}O_2$
M_r/g mol^{-1}	178.228
crystal size/mm	0.13 × 0.08 × 0.03
T/K	100(2)
radiation	'Mo Kα
diffractometer	'Bruker D8Venture'
crystal system	monoclinic
space group	$P2_1/n$
a/Å	10.9424(4)
b/Å	6.3342(3)
c/Å	13.8520(5)
α/°	90
β/°	113.130(2)
γ/°	90
V/Å^3	882.93(6)
Z	4
calc. density/g cm^{-3}	1.34080(9)
μ/mm^{-1}	0.091
absorption correction	multi-scan
transmission factor range	0.8817–0.9590
refls. measured	14090
R_{int}	0.0527
mean σ(I)/I	0.0349
θ range	3.03–27.61
observed refls.	1587
x, y (weighting scheme)	0.0480, 0.4016
hydrogen refinement	mixed
refls in refinement	2028
parameters	122
restraints	0
$R(F_{obs})$	0.0428
$R_w(F^2)$	0.1049
S	1.039
shift/error$_{max}$	0.001
max electron density/e Å^{-3}	0.408
min electron density/e Å^{-3}	−0.181

C-bound H: constr, O-bound H: refall.



10 Computational Details

10.1 Thermodynamic calculations

All calculations were performed using Gaussian03.[192] Geometry optimization / single point energy calculation was carried out with the B3LYP[193] functional and the basis set as given below. Figure 36 shows the chemical structures of the calculated compounds.

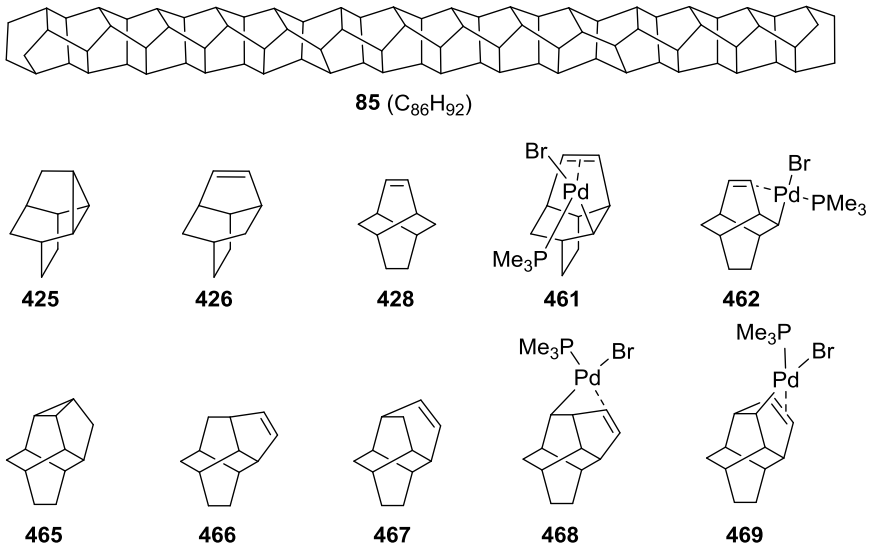


Figure 36. Overview of calculated compounds.

Cartesian coordinates:

85 ($C_{86}H_{92}$) 6-31G(d)
C 7.267697 1.011689 -0.763766
C 7.445497 1.006134 0.796582
C 8.273858 -0.045730 -1.256971
C 8.893226 0.588900 1.151915
C 9.080257 -0.945370 0.875627
C 8.084244 -1.244003 -0.260800
C 9.723353 0.491612 -1.152667
C 9.899396 1.26537 0.202449
C 11.346434 1.077433 0.722829
C 10.727054 -0.672601 -1.049641
C 12.356995 1.187078 -0.434641
C 12.178329 -0.15769 -1.22351
C 10.533125 -1.21341 0.410735
C 11.5281 -0.389733 1.249449
C 5.819023 0.595895 -1.120974
C 6.441906 -0.056315 1.282332
C 4.993042 0.480606 1.184692
C 4.813462 1.263987 -0.164468
C 5.632625 -0.940333 -0.85624
C 6.63084 -1.246698 0.276403
C 3.364493 1.0787 -0.681263
C 3.991614 -0.684251 1.075953
C 4.180625 -1.213374 -0.389402
C 3.180122 -0.384663 -1.217231
C 2.359327 1.179324 0.4815
C 2.541625 -0.172394 1.259932
C 0.910349 1.273831 -0.05709
C 1.541709 -1.129889 0.585809
C 1.728827 -0.857458 -0.949016
C 0.725859 0.272298 -1.251738
C -0.092169 0.779179 1.002467
C 0.092162 -0.780505 1.00175
C -1.541704 1.128955 0.586821
C -0.910354 -1.274189 -0.058269
C -0.725843 -0.271563 -1.251997
C -1.728805 0.857929 -0.94825
C -2.541616 0.170842 1.26007
C -2.359341 -1.180157 0.480387
C -3.991595 0.682901 1.076563
C -3.36452 -1.078442 -0.682268
C -3.180108 0.385408 -1.216894
C -4.180581 1.213385 -0.388302
C -4.993061 -0.482029 1.184229
C -4.813495 -1.264169 -0.165647
C -6.4419 0.054883 1.282354
C -5.819055 -0.59517 -1.121527
C -5.63258 0.940814 -0.855402
C -6.630761 1.246205 0.277521
C -7.44557 -1.007053 0.795642
C -7.267758 -1.011197 -0.764707
C -8.893272 -0.590032 1.151355
C -8.273852 0.04674 -1.256955
C -9.080187 0.944499 0.87647
C -8.084158 1.244095 -0.25969
C -9.899497 -1.26556 0.201267
C -9.723388 -0.490579 -1.153143
C -11.346529 -1.077985 0.721816
C -10.726999 0.673608 -1.049052
C -10.533029 1.213069 0.411821
C -11.528063 0.38871 1.249787
C -12.357116 -1.186483 -0.435753
C -12.178314 0.158984 -1.223393
C -13.801613 -1.279771 0.114794
C -13.176909 1.117058 -0.549546
C -12.979575 0.860297 0.986688
C -13.978046 -0.265837 1.306825
C -14.820577 -0.79898 -0.939864
C -14.629991 0.761411 -0.945867
C -16.275817 -1.150558 -0.49967
C -15.618746 1.267043 0.125262
C -15.443508 0.256424 1.3142
C -16.359642 -0.953816 1.034355
C -17.043535 1.229063 -0.45987
C -17.266324 -0.153815 -1.133482
C 13.80148 1.280015 0.115963
C 13.177012 -1.116288 -0.550531
C 12.979666 -0.860932 0.985929
C 13.978036 0.265017 1.30707
C 14.630052 -0.760133 -0.946553
C 14.820461 0.800276 -0.939156
C 16.275667 1.15162 -0.498691
C 15.618893 -1.266606 0.124101
C 17.043672 -1.22793 -0.461024
C 15.443561 -0.25708 1.313948
C 16.359557 0.953505 1.035159
C 17.266271 0.155564 -1.133429
H 7.485347 2.000472 -1.187569
H 7.226287 1.991448 1.227598
H 8.063632 -0.347736 -2.291046
H 9.103454 0.834837 2.200763
H 8.861183 -1.542974 1.769825
H 8.302876 -2.20494 -0.744121
H 9.943742 1.136026 -2.013298
H 9.68293 2.334869 0.084034
H 11.556417 1.813759 1.509309
H 10.517242 -1.450098 -1.795484
H 12.145446 2.056375 -1.070355
H 12.401913 -0.029367 -2.290446
H 10.750076 -2.287627 0.471974
H 11.304096 -0.460868 2.321593
H 5.607138 0.850229 -2.167488
H 6.653962 -0.366514 2.31361

H 4.773744 1.118606 2.050365
H 5.028786 2.332859 -0.038481
H 5.850473 -1.53129 -1.755144
H 6.41371 -2.211435 0.752768
H 3.150772 1.820675 -1.461415
H 4.205527 -1.46728 1.814848
H 3.965321 -2.28746 -0.458031
H 3.398249 -0.448388 -2.291055
H 2.574066 2.043112 1.123592
H 2.323235 -0.051402 2.328768
H 0.694431 2.305644 -0.362776
H 1.757711 -2.176674 0.835521
H 1.515585 -1.754724 -1.544139
H 0.941588 0.753359 -2.214456
H 0.124429 1.206868 1.989805
H -0.12445 -1.209104 1.98869
H -1.757706 2.175514 0.837478
H -0.694442 -2.305721 -0.364899
H -0.941559 -0.751745 -2.215154
H -1.515547 1.755733 -1.542553
H -2.323221 0.048866 2.328792
H -2.574106 -2.044529 1.121686
H -4.205479 1.465256 1.816182
H -3.150806 -1.819706 -1.463102
H -3.398237 0.450134 -2.290659
H -3.965248 2.287531 -0.455936
H -4.773805 -1.120831 2.049321
H -5.028846 -2.333152 -0.04064
H -6.65394 0.364152 2.313914
H -5.607183 -0.848569 -2.168273
H -5.8504 1.532598 -1.753768
H -6.413567 2.210494 0.754761
H -7.226433 -1.992774 1.225757
H -7.485478 -1.999576 -1.18942
H -9.103527 -0.8369 2.199976
H -8.063591 0.349677 -2.290751
H -8.861066 1.541276 1.77121
H -8.302725 2.205485 -0.742138
H -9.683111 -2.334967 0.081877
H -9.943839 -1.134188 -2.01436
H -11.556561 -1.815012 1.507626
H -10.517115 1.45177 -1.794183
H -10.749895 2.287244 0.474048
H -11.304061 0.458835 2.321998
H -12.145673 -2.055222 -1.072258
H -12.40191 0.031654 -2.290449
H -14.004347 -2.310195 0.431936
H -12.968902 2.162789 -0.810466
H -13.186912 1.763677 1.574466
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H -14.859264 1.187852 -1.931067
H -16.515221 -2.181208 -0.788675
H -15.36797 2.286698 0.442625
H -15.673822 0.734202 2.274449
H -16.01488 -1.83423 1.589583
H -17.396475 -0.774201 1.343791
H -17.169555 2.041518 -1.186238
H -17.783875 1.40223 0.331366
H -18.298896 -0.496015 -0.991812
H -17.100567 -0.091763 -2.216744
H 14.004109 2.310173 0.434029
H 12.969106 -2.161804 -0.812384
H 13.187097 -1.764825 1.572887
H 13.753307 0.739737 2.270931
H 14.859359 -1.185651 -1.932143
H 14.61194 1.233086 -1.92561
H 16.514942 2.182555 -0.78679
H 15.368253 -2.286576 0.44056
H 17.784058 -1.401689 0.330037
H 17.169774 -2.03973 -1.188112
H 15.673958 -0.735693 2.273762
H 17.396419 0.773722 1.344406
H 16.014714 1.833379 1.591194
H 18.298801 0.497767 -0.991472
H 17.100499 0.094457 -2.216742

425 6-31G(d)
C 1.995091 -0.26669 -0.371015
C 0.738812 -0.036243 -1.248186
C 0.182693 1.352512 -0.881427
C 1.637896 0.066109 1.106706
C -0.586814 1.182567 0.451289
C 0.102009 0.037568 1.278396
C -0.279867 -1.124332 -0.864919
C -0.473651 -1.229796 0.634876
C -1.638146 -0.830584 -0.23679
C -1.975901 0.610945 0.106795
H 2.826578 0.358501 -0.720117
H 2.319624 -1.310267 -0.46406
H 0.995433 -0.09648 -2.311956
H -0.491647 1.738022 -1.655919
H 1.00627 2.07212 -0.789371
H 2.110727 -0.647733 1.791733
H 2.019112 1.057558 1.383697
H -0.638108 2.123041 1.010186
H -0.176367 0.110155 2.33679
H -0.213057 -2.055706 -1.423867
H -0.418854 -2.183729 1.153897
H -2.440404 -1.535959 -0.438978
H -2.648931 0.628013 0.975607
H -2.463103 1.170119 -0.701993

425 6-311+G(2d.p)
C 1.99206 -0.262034 -0.372432
C 0.737326 -0.026942 -1.244759
C 0.18158 1.35601 -0.870553
C 1.634602 0.056466 1.105438
C -0.585241 1.177261 0.458569
C 0.101872 0.027667 1.275255
C -0.279058 -1.115581 -0.871465
C -0.473036 -1.232073 0.624909
C -1.635278 -0.826609 -0.242326
C -1.971354 0.60916 0.111633
H 2.818816 0.36662 -0.715166
H 2.317944 -1.300639 -0.474322
H 0.992648 -0.080659 -2.305345
H -0.493022 1.743264 -1.638808
H 1.001715 2.07383 -0.776293
H 2.104528 -0.662315 1.781534
H 2.015843 1.041424 1.391273
H -0.636183 2.109946 1.023249
H -0.175776 0.092298 2.330548
H -0.214028 -2.03939 -1.435504
H -0.421484 -2.187129 1.1339
H -2.433884 -1.528704 -0.448831
H -2.641287 0.619298 0.97858
H -2.456666 1.1722 -0.690434

426 6-31G(d)
C -2.118471 0.000832 -0.028614
C -1.045811 0.002441 -1.133899
C -0.193856 -1.282044 -0.972832
C -1.411228 -0.003233 1.355741
C 0.665179 -1.185034 0.33277
C 0.112877 -0.002465 1.180406
C -0.193074 1.285818 -0.967975
C 0.66526 1.183632 0.337692
C 2.057904 -0.667962 0.002449
C 2.058037 0.667854 0.005524
H -2.76399 0.881428 -0.135472
H -2.76602 -0.877748 -0.13966
H -1.530578 0.004448 -2.118582
H 0.456622 -1.433113 -1.842829
H -0.868993 -2.147062 -0.929742
H -1.706282 -0.881763 1.943478
H -1.706968 0.871262 1.949094
H 0.668097 -2.137919 0.874848
H 0.605952 -0.004466 2.15963
H 0.458017 1.439393 -1.837073
H -0.867603 2.15118 -0.92234
H 0.668018 2.134293 0.883649
H 2.886294 -1.312733 -0.279279
H 2.88653 1.313758 -0.273291

426 6-311+G(2d.p)
C -2.114577 0.000271 -0.029753
C -1.04331 0.000671 -1.131573
C -0.193549 -1.281285 -0.968187
C -1.408535 -0.000881 1.352083
C 0.664241 -1.181886 0.33438
C 0.112001 -0.00065 1.178308
C -0.193255 1.282305 -0.9669
C 0.664318 1.181514 0.335722
C 2.053382 -0.665117 0.002691
C 2.053466 0.665024 0.003579
H -2.758221 0.877565 -0.137463
H -2.758846 -0.876419 -0.138612
H -1.525174 0.001229 -2.113508
H 0.45527 -1.434966 -1.834418
H -0.866833 -2.14292 -0.921912
H -1.703768 -0.875069 1.939636
H -1.704054 0.872111 1.94125
H 0.670565 -2.130752 0.875601
H 0.602718 -0.0012 2.154795
H 0.455755 1.436606 -1.832875
H -0.866348 2.144054 -0.919987
H 0.670636 2.129778 0.877986
H 2.881528 -1.305346 -0.277161
H 2.881684 1.305531 -0.275427

428 6-31G(d)
C 0.56109 -1.080918 -0.688228
C 1.945524 -0.527237 -0.41283
C 1.945501 0.527307 0.41278
C 0.561032 1.080934 0.688215
C 0.026932 -1.403408 0.743969
C -0.406833 -0.02758 1.29158
C -1.845136 0.177855 0.759955
C -1.845148 -0.177941 -0.759914
C -0.406892 0.027568 -1.291573
C 0.026771 1.40342 -0.74396
H 0.57987 -1.967605 -1.329575
H 2.842143 -1.026089 -0.772347
H 2.842077 1.026256 0.772275
H 0.579806 1.967627 1.329551
H -0.824652 -2.093947 0.729295
H 0.815853 -1.87054 1.339225
H -0.379681 0.007417 2.385489
H -2.541011 -0.467996 1.30881
H -2.180678 1.208977 0.923029
H -2.541062 0.46789 -1.308741
H -2.180663 -1.209069 -0.923001
H -0.379802 -0.007416 -2.385483
H -0.824885 2.093875 -0.729256
H 0.81563 1.87061 -1.339244

428 6-311+G(2d.p)
C 0.560788 -1.072809 -0.696054
C 1.940928 -0.523727 -0.41277
C 1.940928 0.523725 0.412767
C 0.560789 1.072808 0.696056
C 0.025324 -1.408112 0.729376
C -0.40582 -0.040045 1.288323
C -1.840683 0.171879 0.759876
C -1.840682 -0.17188 -0.759879
C -0.405819 0.040047 -1.288322
C 0.025324 1.408114 -0.729373
H 0.581405 -1.949372 -1.344692

H 2.837589 -1.012514 -0.7759
H 2.83759 1.012514 0.775894
H 0.581411 1.949371 1.344695
H -0.824909 -2.093961 0.70601
H 0.810053 -1.882175 1.318111
H -0.377759 -0.013945 2.378595
H -2.535055 -0.475739 1.301198
H -2.174562 1.198519 0.930517
H -2.535055 0.475736 -1.301201
H -2.174558 -1.198521 -0.93052
H -0.377752 0.013948 -2.378595
H -0.824913 2.093958 -0.706002
H 0.810048 1.882183 -1.318108

461 6-31G(d)/SDD
Pd 0.313695 -0.207617 -0.215524
Br 2.246324 -1.832655 0.2634
P 1.764616 1.583225 -0.048465
C -1.374411 -1.931648 0.013217
C -1.252553 -1.42795 -1.255652
C -2.212085 -0.235311 -1.359064
C -1.428176 0.868538 -0.582151
C -2.120482 1.180155 0.76041
C -3.57426 1.621101 0.467178
C -4.361186 0.40106 -0.086186
C -3.38623 -0.71777 -0.474292
C -2.571111 -1.291982 0.731659
C -2.17922 -0.095294 1.642721
C 1.119263 3.29773 -0.296092
C 2.608565 1.685121 1.58736
C 3.158467 1.486411 -1.249859
H -0.823415 -2.779639 0.406529
H -0.638844 -1.831243 -2.055734
H -2.494062 0.047464 -2.378167
H -1.258381 1.772224 -1.17341
H -1.586056 1.980957 1.286275
H -3.569182 2.442726 -0.260271
H -4.044513 2.010438 1.379162
H -5.067302 0.020524 0.663178
H -4.964521 0.685713 -0.956649
H -3.91297 -1.535375 -0.983147
H -3.123985 -2.046291 1.30332
H -1.219709 -0.285922 2.136435
H -2.929235 0.039643 2.433627
H 0.326231 3.50801 0.428197
H 0.698342 3.39596 -1.301544
H 1.91796 4.037858 -0.173244
H 1.872659 1.881569 2.373315
H 3.364704 2.478848 1.593908
H 3.07726 0.717522 1.785795
H 3.643594 0.514292 -1.128973
H 3.881032 2.293273 -1.081194
H 2.770353 1.555406 -2.270819

461 6-311+G(2d.p)/SDD
Pd 0.31335 -0.201873 -0.219775
Br 2.265289 -1.837453 0.264626
P 1.758303 1.593377 -0.047725
C -1.379932 -1.935087 0.001438
C -1.255499 -1.423051 -1.254909
C -2.212723 -0.233353 -1.354489
C -1.435865 0.867452 -0.574109
C -2.124175 1.165023 0.768674
C -3.575407 1.606772 0.480742
C -4.358984 0.393951 -0.08486
C -3.38635 -0.719599 -0.476956
C -2.573154 -1.301615 0.722662
C -2.18107 -0.114397 1.639379
C 1.109327 3.293414 -0.311915
C 2.577629 1.707149 1.589194
C 3.156321 1.495541 -1.22921
H -0.829773 -2.783215 0.386569
H -0.639348 -1.818384 -2.052206
H -2.490662 0.053557 -2.369639
H -1.270344 1.771424 -1.158106
H -1.593077 1.959462 1.299193
H -3.571886 2.433516 -0.235364
H -4.044203 1.983869 1.394265
H -5.067987 0.01074 0.655319
H -4.955767 0.686072 -0.952982
H -3.91019 -1.531211 -0.990685
H -3.124022 -2.057861 1.286823
H -1.224047 -0.307349 2.12859
H -2.926374 0.014468 2.430686
H 0.313221 3.504243 0.402858
H 0.699282 3.380071 -1.318678
H 1.904337 4.031948 -0.187765
H 1.831106 1.896378 2.36139
H 3.318989 2.509701 1.598334
H 3.057117 0.750417 1.795038
H 3.650403 0.534027 -1.092682
H 3.862971 2.311653 -1.061404
H 2.775758 1.54965 -2.249779

461 6-311+G(2d.p)/LANL2DZ
Pd 0.310939 -0.201566 -0.226792
Br 2.289297 -1.838194 0.267325
P 1.755653 1.603304 -0.048726
C -1.40243 -1.951231 -0.00104
C -1.274106 -1.43624 -1.253759
C -2.223909 -0.239885 -1.352969
C -1.444574 0.861366 -0.578157
C -2.120773 1.158211 0.7691
C -3.571867 1.607279 0.491295
C -4.363311 0.400518 -0.076379
C -3.398586 -0.71859 -0.472006
C -2.586262 -1.307166 0.724601
C -2.178197 -0.122347 1.638454
C 1.10404 3.301242 -0.317233
C 2.564046 1.716003 1.593096
C 3.160049 1.504546 -1.221442
H -0.850955 -2.798149 0.385111
H -0.653248 -1.828374 -2.048989
H -2.502846 0.045891 -2.368166
H -1.278324 1.764292 -1.162887
H -1.582873 1.949352 1.297585
H -3.569201 2.437808 -0.220394
H -4.033501 1.981529 1.409559
H -5.074128 0.020078 0.663432
H -4.958925 0.698304 -0.943357
H -3.928977 -1.526216 -0.985188
H -3.14218 -2.056801 1.292525
H -1.218563 -0.322019 2.119686
H -2.915998 0.010919 2.435943
H 0.302282 3.509636 0.391946
H 0.700707 3.386212 -1.326896
H 1.895246 4.04303 -0.188044
H 1.812607 1.905331 2.360465
H 3.306312 2.517695 1.607878
H 3.040673 0.758251 1.800846
H 3.65222 0.542728 -1.080173
H 3.866247 2.320592 -1.051036
H 2.785341 1.556937 -2.244262

462 6-31G(d)/SDD
C 2.114575 -0.056245 -1.29446
C 3.636928 -0.200086 -0.901277
C 3.732305 -1.175741 0.290123
C 1.394591 0.861139 -0.257392
C 2.425828 -0.923036 1.110589
C 2.146213 0.629341 1.058704
C 4.136523 1.16767 -0.391173
C 3.462976 1.440305 0.984763
H 1.994894 0.29759 -2.321849
H 4.221203 -0.545284 -1.760899
H 4.62912 -0.969585 0.885928
H 3.786928 -2.223678 -0.022259
H 1.317164 1.911686 -0.546945
H 1.560944 0.92696 1.934519
H 5.228882 1.164287 -0.296606
H 3.884246 1.95672 -1.110603
H 4.129019 1.161583 1.811814
H 3.246453 2.508309 1.107193
C 1.363772 -1.678137 0.318648
C 1.316147 -1.323882 -1.014586
H 2.504399 -1.286017 2.139022
H -0.571904 3.505377 0.686176
H -0.733109 3.444445 -1.0785
H -2.092621 4.02415 -0.083664
C -1.268193 3.303939 -0.133985
H -2.669927 1.601508 -2.331682
H -3.626689 0.501465 -1.320279
H -3.912834 2.271438 -1.237132
H -3.365816 0.605888 1.639539
H -2.250832 1.765802 2.388163
H -3.670396 2.36774 1.4866
C -3.156064 1.487576 -1.357738
C -2.900298 1.588517 1.525159
P -1.892142 1.567026 -0.018385
Br -2.288918 -1.882167 0.123319
Pd -0.376021 -0.192029 -0.098881
H 0.920385 -2.594297 0.697145
H 0.829904 -1.920469 -1.781785

462 6-311+G(2d.p)/SDD
C 2.115432 -0.062662 -1.28981
C 3.635793 -0.210399 -0.89784
C 3.729738 -1.183356 0.290828
C 1.402181 0.857705 -0.257117
C 2.424746 -0.926802 1.107721
C 2.150432 0.623636 1.0547
C 4.139901 1.152691 -0.391158
C 3.466704 1.429317 0.980745
H 1.9978 0.288564 -2.314213
H 4.215361 -0.55641 -1.75562
H 4.623924 -0.979697 0.884604
H 3.779958 -2.228255 -0.01935
H 1.326008 1.903632 -0.546953
H 1.569043 0.922305 1.92778
H 5.228457 1.144391 -0.294614
H 3.893895 1.939517 -1.109707
H 4.1287 1.152073 1.806735
H 3.253275 2.494526 1.099995
C 1.367151 -1.679094 0.316189
C 1.31718 -1.32429 -1.008426
H 2.500288 -1.287352 2.133213
H -0.560321 3.495022 0.689618
H -0.71867 3.436395 -1.071059
H -2.073671 4.019603 -0.080287
C -1.253062 3.300474 -0.130019
H -2.649734 1.611823 -2.32089
H -3.622143 0.528815 -1.313026
H -3.882912 2.297698 -1.233739
H -3.365016 0.628316 1.629218
H -2.234431 1.766696 2.377695
H -3.64189 2.390079 1.481823
C -3.140122 1.505397 -1.352547
C -2.886784 1.601374 1.519383
P -1.885379 1.576656 -0.01716
Br -2.310068 -1.885305 0.123309
Pd -0.374027 -0.187472 -0.100118
H 0.923712 -2.592727 0.691577
H 0.830978 -1.919409 -1.771678

462 6-311+G(2d.p)/LANL2DZ
C 2.126781 -0.073149 -1.289543
C 3.647534 -0.213337 -0.8935
C 3.743189 -1.183516 0.29713
C 1.412361 0.848811 -0.262066

C 2.434499 -0.931619 1.109978
C 2.153238 0.617755 1.053094
C 4.144564 1.152681 -0.387108
C 3.46671 1.428431 0.982871
H 2.010155 0.274242 -2.315296
H 4.230442 -0.557869 -1.749526
H 4.634613 -0.973901 0.892968
H 3.799699 -2.228802 -0.010373
H 1.332448 1.893323 -0.554456
H 1.566271 0.914655 1.922914
H 5.232837 1.148772 -0.287642
H 3.89744 1.93767 -1.107246
H 4.126977 1.15394 1.811074
H 3.249325 2.492969 1.100544
C 1.383966 -1.691188 0.317393
C 1.33317 -1.337778 -1.005834
H 2.509533 -1.288979 2.136559
H -0.552438 3.499399 0.69367
H -0.711806 3.44615 -1.067285
H -2.064049 4.031211 -0.074294
C -1.246064 3.30921 -0.126288
H -2.647855 1.625536 -2.32071
H -3.620347 0.542947 -1.312501
H -3.879706 2.31232 -1.232477
H -3.359423 0.633756 1.626054
H -2.229744 1.771108 2.377531
H -3.638439 2.39605 1.484494
C -3.137793 1.519265 -1.352139
C -2.88263 1.60784 1.519247
P -1.882601 1.586998 -0.017678
Br -2.339279 -1.883205 0.124409
Pd -0.370217 -0.189227 -0.104577
H 0.937481 -2.602058 0.695747
H 0.84318 -1.931223 -1.767786

465 6-31G(d)
C -0.056778 -0.646854 -1.253142
C -0.439787 0.840558 -0.947907
C 0.310731 1.225431 0.346601
C -0.994049 -1.54521 -0.401303
C 0.20134 -0.055491 1.251928
C -1.155305 -0.78051 0.935478
C -1.948842 0.983168 -0.657237
C -2.258282 0.27358 0.693658
C 1.34942 -0.989361 -0.727681
C 1.806395 1.426858 0.069246
C 1.413119 -0.876135 0.784847
C 2.293894 0.001485 -0.078795
H -0.146081 -0.862769 -2.32382
H -0.141757 1.492991 -1.777945
H -0.144636 2.109652 0.806755
H -0.543722 -2.534729 -0.265455
H -1.972974 -1.700184 -0.871528
H 0.265755 0.199996 2.316371
H -1.428892 -1.453292 1.75645
H -2.217001 2.045742 -0.607939
H -2.541308 0.549824 -1.472489
H -2.283944 0.997021 1.518476
H -3.244392 -0.205845 0.664369
H 1.810078 -1.86513 -1.181304
H 2.312444 1.908681 0.917344
H 1.975441 2.052354 -0.817344
H 1.810072 -1.679792 1.399703
H 3.359787 -0.199637 -0.155807

465 6-311+G(2d.p)
C -0.056106 -0.644845 -1.249629
C -0.439177 0.839526 -0.944882
C 0.310576 1.223785 0.345634
C -0.992918 -1.542027 -0.40197
C 0.201021 -0.055386 1.248484
C -1.152959 -0.779309 0.932441
C -1.944924 0.981912 -0.655006
C -2.254515 0.27164 0.692455
C 1.34694 -0.987368 -0.726094
C 1.802742 1.423072 0.068928
C 1.409983 -0.874531 0.783975
C 2.289642 0.001468 -0.078476
H -0.143231 -0.859426 -2.316962
H -0.142455 1.489795 -1.772155
H -0.141987 2.105301 0.804731
H -0.544507 -2.528694 -0.268313
H -1.968735 -1.694117 -0.870818
H 0.264467 0.197787 2.309775
H -1.424279 -1.449893 1.750988
H -2.211473 2.041085 -0.603381
H -2.53624 0.551996 -1.468118
H -2.282446 0.991372 1.515718
H -3.236551 -0.207824 0.660913
H 1.80741 -1.859208 -1.178097
H 2.307074 1.90341 0.914521
H 1.97131 2.045409 -0.815491
H 1.80833 -1.674512 1.395791
H 3.351476 -0.200097 -0.154266

466 6-31G(d)
C 0.306949 0.999668 -1.071784
C 0.456947 -0.575583 -1.135105
C -0.395471 -1.245841 -0.007466
C 1.203473 1.525638 0.075489
C -0.323371 -0.184409 1.12493
C 1.109363 0.439141 1.159899
C 1.916005 -0.948674 -0.778054
C 2.137241 -0.640564 0.736133
C -1.112626 1.454494 -0.680542
C -1.88649 -1.407088 -0.215409
C -1.516814 0.721918 0.650474
C -2.534354 -0.337601 0.251858
H 0.598884 1.433163 -2.036424
H 0.184223 -0.944367 -2.130687
H 0.067105 -2.204155 0.259522
H 0.838376 2.499169 0.423655
H 2.246544 1.673131 -0.229778
H -0.577569 -0.634638 2.091623
H 1.342868 0.828553 2.157362
H 2.095886 -2.010321 -0.986989
H 2.62047 -0.381927 -1.399143
H 2.020979 -1.547424 1.341676
H 3.155586 -0.272996 0.911605
H -1.109394 2.544434 -0.554905
H -1.843133 1.229316 -1.465155
H -2.333943 -2.282592 -0.678019
H -1.86616 1.42324 1.415348
H -3.605837 -0.159183 0.217775

466 6-311+G(2d.p)
C 0.305982 0.997708 -1.06936
C 0.455324 -0.575158 -1.132006
C -0.395 -1.243424 -0.006434
C 1.201754 1.522917 0.074351
C -0.322035 -0.18384 1.123021
C 1.107859 0.43874 1.156183
C 1.911077 -0.948413 -0.776945
C 2.133432 -0.639219 0.734147
C -1.109434 1.45281 -0.678029
C -1.882918 -1.403066 -0.213654
C -1.514056 0.720254 0.64969
C -2.528216 -0.337039 0.248943
H 0.595796 1.428557 -2.031573
H 0.1822 -0.943059 -2.123673
H 0.06392 -2.199268 0.259019
H 0.836924 2.493147 0.420209
H 2.24133 1.669144 -0.23001
H -0.573713 -0.631498 2.087579
H 1.340325 0.826573 2.150368
H 2.088417 -2.007248 -0.983166
H 2.613629 -0.385504 -1.397273
H 2.018647 -1.542528 1.338811
H 3.148525 -0.272192 0.906894
H -1.103429 2.538516 -0.548931
H -1.839619 1.23141 -1.458971
H -2.332902 -2.273791 -0.675032
H -1.865598 1.417443 1.41172
H -3.597073 -0.163316 0.214594

467 6-31G(d)
C 0.107163 0.314633 1.296029
C -0.314537 -1.064534 0.684666
C 0.349985 -1.052125 -0.729153
C -0.965238 1.330371 0.846683
C 0.039351 0.41408 -1.266508
C -1.29395 0.921998 -0.6191
C -1.838106 -1.219746 0.524681
C -2.330817 -0.211309 -0.547139
C 1.491673 0.76539 0.662525
C 1.81643 -1.304205 -0.47003
C 1.156043 1.341211 -0.756444
C 2.381464 -0.418921 0.360197
H 0.19301 0.258362 2.386265
H 0.088454 -1.890136 1.278695
H -0.090654 -1.812166 -1.382699
H -0.599163 2.359155 0.93093
H -1.865611 1.271442 1.469712
H -0.038731 0.413423 -2.35901
H -1.676412 1.772596 -1.196322
H -2.071093 -2.250472 0.230387
H -2.342383 -1.051055 1.484529
H -2.432642 -0.697335 -1.526202
H -3.320182 0.185611 -0.288444
H 1.975484 1.510012 1.3028
H 2.313081 -2.194679 -0.847567
H 0.812093 2.381072 -0.722911
H 2.048132 1.31409 -1.387701
H 3.409853 -0.470983 0.709096

467 6-311+G(2d.p)
C 0.107124 0.311131 1.293688
C -0.31551 -1.064085 0.681642
C 0.34978 -1.049612 -0.728506
C -0.962259 1.326193 0.847587
C 0.039943 0.415713 -1.262826
C -1.29091 0.921079 -0.615853
C -1.835344 -1.217702 0.520722
C -2.326601 -0.208493 -0.5469
C 1.48951 0.762167 0.661613
C 1.811463 -1.30151 -0.467378
C 1.153601 1.340759 -0.753288
C 2.376391 -0.418 0.355502
H 0.194491 0.253374 2.379905
H 0.085114 -1.888589 1.271907
H -0.087021 -1.80637 -1.381887
H -0.595934 2.350823 0.93262
H -1.859886 1.26709 1.467929
H -0.03827 0.415786 -2.351503
H -1.6712 1.770049 -1.189783
H -2.067707 -2.244198 0.224483
H -2.338383 -1.05189 1.477667
H -2.429684 -0.6908 -1.523722
H -3.312013 0.187683 -0.287068
H 1.973209 1.501263 1.301854
H 2.310733 -2.18631 -0.845251
H 0.809065 2.376253 -0.715767
H 2.043351 1.316048 -1.381625
H 3.401005 -0.476038 0.704227

468 6-31G(d)/SDD
Pd 0.632376 -0.207039 -0.287272
Br 2.484655 -1.85135 0.410286
P 2.08912 1.569334 0.068148

C -0.998605 -1.87253 -0.334688
C -0.794423 -1.338557 -1.585168
C -1.765813 -0.160746 -1.728107
C -1.03798 0.893427 -0.834525
C -1.905943 1.20058 0.395321
C -3.261475 1.683335 -0.188708
C -4.036185 0.386151 -0.495555
C -4.662037 -0.063352 0.846098
C -3.554768 -0.000225 1.940226
C -2.174969 -0.097474 1.250163
C -2.280432 -1.304304 0.273566
C -3.013791 -0.690586 -0.962973
C 3.593257 1.466143 -0.992323
C 1.500083 3.299281 -0.214183
C 2.765987 1.632594 1.78122
H -0.48437 -2.739401 0.066011
H -0.120488 -1.710391 -2.350841
H -1.955879 0.166847 -2.754377
H -0.773694 1.80269 -1.380047
H -1.4439 1.972057 1.0231
H -3.823596 2.312641 0.513142
H -3.089717 2.288167 -1.087649
H -4.810553 0.542013 -1.255235
H -5.069032 -1.078522 0.759195
H -5.502694 0.591143 1.10583
H -3.624499 0.933414 2.511933
H -3.672206 -0.818338 2.660959
H -1.376244 -0.243543 1.985304
H -2.840966 -2.113041 0.757457
H -3.504904 -1.476667 -1.55099
H 4.049679 0.484743 -0.838944
H 3.306967 1.553617 -2.045096
H 4.30874 2.25881 -0.744428
H 1.179675 3.419316 -1.253819
H 0.644734 3.513752 0.433997
H 2.294914 4.023841 -0.004101
H 1.95794 1.837706 2.490555
H 3.5358 2.407041 1.87642
H 3.187829 0.650721 2.011729

468 6-311+G(2d.p)/SDD
Pd 0.632081 -0.201746 -0.29049
Br 2.506494 -1.855853 0.408322
P 2.082898 1.579326 0.069103
C -1.003046 -1.872974 -0.331831
C -0.798595 -1.341548 -1.574441
C -1.767674 -0.167513 -1.720901
C -1.046579 0.889497 -0.8316
C -1.912156 1.193201 0.394907
C -3.265217 1.673284 -0.188937
C -4.035653 0.377417 -0.494289
C -4.661703 -0.070222 0.843867
C -3.556986 -0.007491 1.936396
C -2.17986 -0.102321 1.248859
C -2.281523 -1.307118 0.275638
C -3.014016 -0.695998 -0.95868
C 3.586667 1.478505 -0.975453
C 1.489912 3.295717 -0.224744
C 2.739261 1.652552 1.779673
H -0.487906 -2.735937 0.06731
H -0.124523 -1.712541 -2.335231
H -1.954709 0.157432 -2.74469
H -0.785395 1.794695 -1.376727
H -1.454527 1.962745 1.021228
H -3.826641 2.300094 0.50993
H -3.093579 2.275615 -1.084992
H -4.806924 0.530554 -1.252461
H -5.068823 -1.081568 0.757899
H -5.498877 0.583206 1.102307
H -3.628323 0.921582 2.508414
H -3.673443 -0.824404 2.65309
H -1.384579 -0.244677 1.982571
H -2.838279 -2.11441 0.758032
H -3.502296 -1.480065 -1.545014
H 4.051794 0.507209 -0.809551
H 3.304698 1.553915 -2.026331
H 4.286799 2.280409 -0.729629
H 1.175512 3.406328 -1.263134
H 0.635402 3.509447 0.418128
H 2.281756 4.018404 -0.015747
H 1.922895 1.848191 2.476112
H 3.492892 2.437515 1.875911
H 3.17359 0.681624 2.016503

468 6-311+G(2d.p)/LANL2DZ
Pd 0.628206 -0.200661 -0.296421
Br 2.527946 -1.857647 0.412159
P 2.082796 1.588826 0.067513
C -1.01793 -1.883818 -0.335958
C -0.814884 -1.352308 -1.577019
C -1.780023 -0.174277 -1.721723
C -1.056846 0.884297 -0.838119
C -1.912923 1.188747 0.392743
C -3.267865 1.671854 -0.184765
C -4.042522 0.377595 -0.485633
C -4.662848 -0.067621 0.856087
C -3.552424 -0.006682 1.943012
C -2.179262 -0.106127 1.248371
C -2.290402 -1.311968 0.276855
C -3.025609 -0.698628 -0.95447
C 3.586462 1.4861 -0.976062
C 1.488872 3.304861 -0.224465
C 2.738232 1.657233 1.778138
H -0.498761 -2.743568 0.064976
H -0.137728 -1.719952 -2.336551
H -1.969803 0.148997 -2.745524
H -0.793119 1.787438 -1.38472
H -1.450545 1.957559 1.016267
H -3.823904 2.300477 0.51668
H -3.099303 2.273438 -1.08193
H -4.817242 0.531995 -1.239972
H -5.072894 -1.077995 0.772972
H -5.497105 0.588027 1.11822
H -3.618297 0.923157 2.514424
H -3.667406 -0.822515 2.661113
H -1.380158 -0.250436 1.977459
H -2.848726 -2.115733 0.763187
H -3.518192 -1.481029 -1.539309
H 4.048252 0.513287 -0.80955
H 3.305278 1.56206 -2.02711
H 4.28868 2.286118 -0.729853
H 1.17377 3.415718 -1.262671
H 0.634412 3.51708 0.419021
H 2.279474 4.028986 -0.01561
H 1.921928 1.85192 2.474895
H 3.493248 2.440584 1.877122
H 3.170427 0.684523 2.011609

469 6-31G(d)/SDD
C 1.652861 -0.123188 -1.565204
C 3.201642 -0.242755 -1.296873
C 3.431429 -1.123259 -0.024088
C 1.032897 0.844375 -0.504342
C 2.146931 -0.895158 0.837484
C 1.90396 0.661657 0.740772
C 3.684668 1.184207 -0.960264
C 3.274768 1.393924 0.521418
C 4.6541 -0.669688 0.796476
C 4.364976 0.735937 1.389256
C 1.045508 -1.683268 0.153353
C 0.886691 -1.378229 -1.181006
C -1.57939 3.303979 -0.104525
C -3.586886 1.507876 -1.1553
C -3.065199 1.594553 1.693291
P -2.205302 1.572284 0.062882
Pd -0.720324 -0.197409 -0.156869
H 1.45224 0.196817 -2.591317
H 3.713329 -0.662886 -2.169555
H 3.525919 -2.180555 -0.294221
H 0.926128 1.880166 -0.833297
H 2.291735 -1.225004 1.870476
H 1.425386 1.027527 1.654962
H 4.769547 1.292917 -1.077909
H 3.220934 1.917559 -1.630068
H 3.165952 2.457759 0.763724
H 4.853344 -1.397964 1.591685
H 5.547913 -0.650711 0.160922
H 5.272835 1.351394 1.395459
H 4.027429 0.660992 2.431027
H 0.636477 -2.58394 0.60147
H 0.341375 -2.001707 -1.884332
H -0.804818 3.493948 0.645103
H -1.137566 3.446108 -1.095834
H -2.388534 4.030748 0.029753
H -3.189867 1.626539 -2.168313
H -4.057375 0.523739 -1.081797
H -4.324681 2.294841 -0.9607
H -3.52061 0.612622 1.847161
H -2.338072 1.767382 2.492906
H -3.832727 2.376551 1.726983
Br -2.618731 -1.869259 0.251593

469 6-311+G(2d.p)/SDD
C 1.656315 -0.130485 -1.56099
C 3.202235 -0.252561 -1.290646
C 3.428661 -1.127804 -0.017424
C 1.040462 0.841046 -0.507524
C 2.143472 -0.896315 0.836683
C 1.90499 0.658029 0.73563
C 3.68795 1.17074 -0.959359
C 3.275549 1.385448 0.517711
C 4.646509 -0.675046 0.803638
C 4.360153 0.731183 1.388458
C 1.048447 -1.682925 0.151303
C 0.890748 -1.379409 -1.175193
C -1.56387 3.300153 -0.110643
C -3.578816 1.523314 -1.14034
C -3.037806 1.611021 1.692968
P -2.197043 1.582105 0.063375
Pd -0.718549 -0.193231 -0.162302
H 1.459164 0.185489 -2.58491
H 3.711136 -0.67556 -2.158961
H 3.521504 -2.182471 -0.283068
H 0.935166 1.871654 -0.838443
H 2.283028 -1.222611 1.867504
H 1.428367 1.026578 1.645061
H 4.769817 1.276024 -1.073359
H 3.22962 1.900505 -1.630714
H 3.167447 2.446483 0.755544
H 4.839727 -1.397695 1.600503
H 5.540555 -0.661667 0.174423
H 5.266582 1.342469 1.392144
H 4.023299 0.662413 2.427123
H 0.638875 -2.580927 0.59652
H 0.347647 -2.002659 -1.874909
H -0.787695 3.485287 0.632836
H -1.129522 3.435352 -1.101893
H -2.368491 4.025947 0.02674
H -3.185241 1.632626 -2.151604
H -4.059439 0.548724 -1.057967
H -4.30133 2.318941 -0.944301
H -3.505137 0.639091 1.849515
H -2.301956 1.773793 2.481374
H -3.79015 2.402413 1.73062
Br -2.638688 -1.872899 0.252853

469 6-311+G(2d.p)/LANL2DZ
C 1.66806 -0.139113 -1.563056
C 3.214268 -0.255199 -1.287843

C 3.440406 -1.129899 -0.014337
C 1.050093 0.832028 -0.513374
C 2.151178 -0.904227 0.835442
C 1.906525 0.649407 0.733847
C 3.693783 1.169725 -0.954009
C 3.275083 1.38257 0.52187
C 4.653288 -0.672337 0.811522
C 4.35867 0.732024 1.396524
C 1.063047 -1.695965 0.146314
C 0.906154 -1.39117 -1.17841
C -1.55585 3.308782 -0.112609
C -3.579003 1.5357 -1.137365
C -3.028195 1.619789 1.693979
P -2.193856 1.592878 0.061657
Pd -0.715426 -0.194933 -0.168687
H 1.472879 0.17529 -2.587769
H 3.727101 -0.675599 -2.155037
H 3.538816 -2.184047 -0.279768
H 0.941086 1.861777 -0.84437
H 2.289147 -1.229454 1.866741
H 1.423609 1.015261 1.640922
H 4.775693 1.278497 -1.063809
H 3.235862 1.898387 -1.626827
H 3.161711 2.443043 0.759563
H 4.846708 -1.394876 1.608398
H 5.549558 -0.654539 0.185634
H 5.262466 1.347122 1.404468
H 4.017826 0.660957 2.433716
H 0.650049 -2.592015 0.592189
H 0.360069 -2.011249 -1.878422
H -0.777075 3.490303 0.62909
H -1.123619 3.443235 -1.104924
H -2.356942 4.038008 0.027391
H -3.188487 1.643692 -2.149952
H -4.059348 0.561177 -1.052341
H -4.300564 2.331901 -0.93987
H -3.493893 0.646942 1.84972
H -2.289298 1.781131 2.479822
H -3.780804 2.410752 1.736288
Br -2.667718 -1.870418 0.258084

10.2 NMR calculations

All calculations were performed using Gaussian03.[192] Geometry optimization was carried out at B3LYP/6-31G(d) and NMR chemical shift calculation at B3LYP/6-31+G(d,p)-SCRF level. Figure 37 shows the chemical structures of the compounds used for the linear regression and the calculated oligotwistanes.

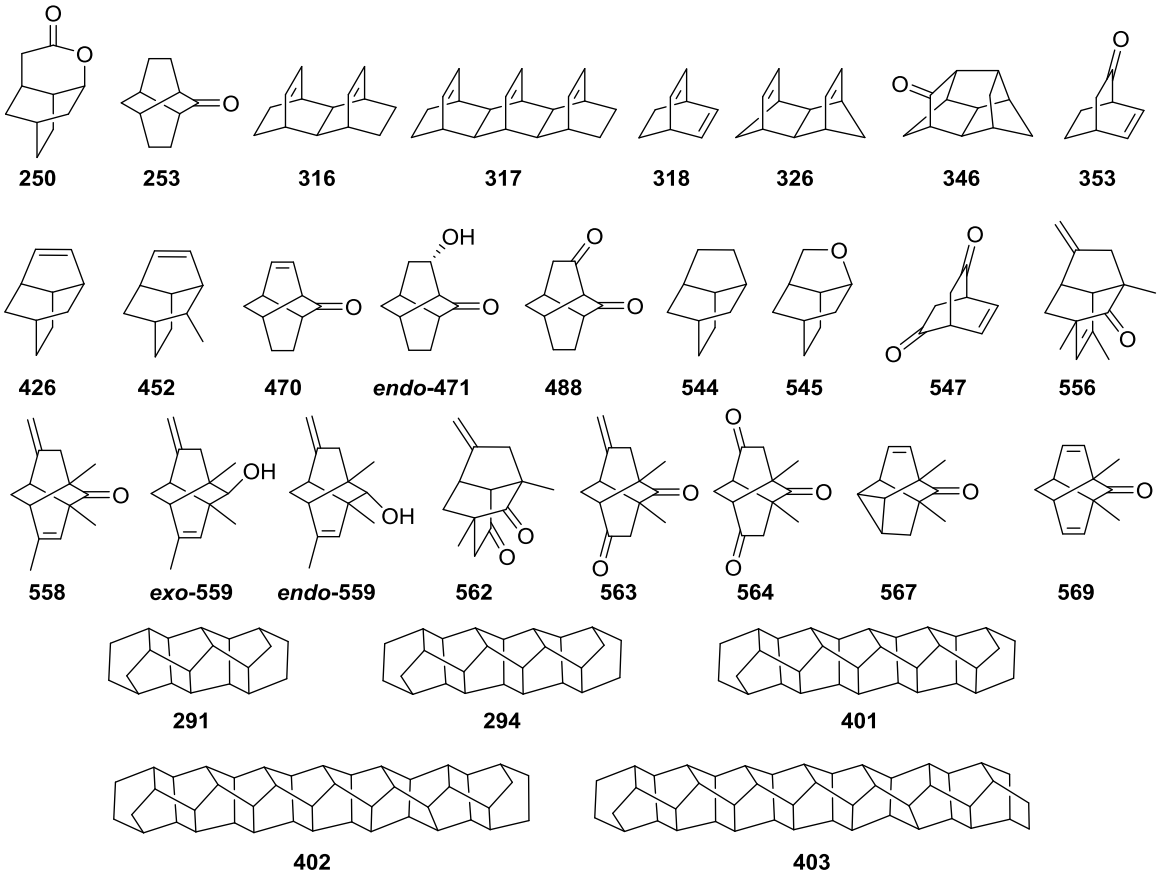

Figure 37. Overview of compounds used for establishing new linear scaling factors and oligotwistanes used for the gradual approximation of the NMR chemical shift of polytwistane (**85**).

Cartesian coordinates:

250
C 0.466916 0.209102 -1.146567
C -0.011113 -1.132014 -0.577580
C 0.767819 -1.449864 0.727325
C -0.000614 1.298538 -0.161331
C 1.554426 -0.205651 1.180495
C 0.594950 0.998783 1.252694
C -2.177864 -0.059493 -0.012669
C 2.652295 0.089062 0.139930
C 2.002624 0.191999 -1.270028
C -1.532239 1.312106 -0.167595
O -3.331032 -0.201348 0.319168
O -1.442915 -1.159883 -0.321178
H 0.011997 0.375573 -2.131233
H 0.124081 -1.931379 -1.311705
H 1.455771 -2.287611 0.559307
H 0.052250 -1.772929 1.490837
H 0.358754 2.274277 -0.511012
H 2.003779 -0.384258 2.164475
H 1.125703 1.878332 1.635860
H -0.209932 0.785885 1.969044
H 3.165906 1.022746 0.399852
H 3.411248 -0.701880 0.159112
H 2.331031 1.100480 -1.787818
H 2.307978 -0.650586 -1.903482
H -1.948520 1.952257 0.616732
H -1.901676 1.713530 -1.121943

253
C -1.910144 -0.412771 0.751429
C -0.477408 -0.853807 1.128109
C 0.001052 -1.797453 0.000131
C -1.909963 0.019476 -0.745575
C 0.478511 -0.853506 -1.128014
C -0.457351 0.407331 -1.142831
C 0.457012 0.408117 1.142653
C -0.000427 1.306626 -0.000300
C 1.910749 -0.410779 -0.751313
C 1.910045 0.021747 0.745630
O -0.002140 2.521309 -0.000030
H -2.619413 -1.231832 0.918297
H -2.227963 0.421081 1.390485
H -0.457117 -1.344600 2.107777
H -0.817381 -2.453514 -0.318526
H 0.820193 -2.452571 0.318907
H -2.581863 0.867865 -0.908944
H -2.257344 -0.795134 -1.392262
H 0.458791 -1.344500 -2.107594
H -0.422938 0.939548 -2.098073
H 0.421880 0.940547 2.097754
H 2.620948 -1.229071 -0.918000
H 2.227662 0.423314 -1.390503
H 2.258196 -0.792370 1.392522
H 2.581017 0.870889 0.908891

316
C -2.474664 -0.778070 -0.915019
C -1.334167 -1.290691 0.014920
C -2.474769 0.779113 -0.913978
C -1.333927 1.290599 0.016239
H -3.435429 -1.166953 -0.561675
H -2.324559 -1.168063 -1.929859
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H -2.325210 1.170493 -1.928358

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C 2.474824 -0.778723 -0.914251
C -0.000011 0.782021 -0.614342
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H 1.338123 2.386091 0.055111
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H -1.714619 1.274968 2.262464
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H 1.715182 1.276301 2.261711

317
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C 3.083942 1.184066 0.668218
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C 1.239636 -0.556867 0.782232
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C 0.000004 1.627665 0.667278
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C -1.239636 -0.556865 0.782232
C -3.643144 -1.210075 0.778695
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C -3.083947 1.184062 -0.668225
C -3.083947 1.184065 0.668220
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H 2.659831 -0.084259 -2.386137
H 1.099078 -1.585053 -1.143240
H 4.645047 -0.999294 1.167154
H 3.347585 -2.192078 1.169558
H 0.000000 0.291522 -2.386055
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H 3.363062 2.040815 -1.276454
H 3.363061 2.040823 1.276441
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H -2.659832 -0.084245 2.386137
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318
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C 0.667738 -1.238295 -0.749684
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C -0.667574 -1.238387 -0.749669
C -1.281844 -0.000079 -0.113416
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H 1.288333 -2.050090 -1.118464
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H -1.168845 -0.883146 1.894503
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H -1.288322 2.050142 -1.118382

326
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346
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353
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C 0.665260 1.183632 0.337692
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H 0.456622 -1.433113 -1.842829
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H 0.605952 -0.004466 2.159630
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H 2.886294 -1.312734 -0.279279
H 2.886530 1.313757 -0.273291

452
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C -0.526866 -1.005762 -1.358494
C 0.691434 -1.334137 1.291548
C -1.456847 -0.869816 -0.104984
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C 2.095576 1.644746 -0.076089
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470
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H -2.172826 0.351842 1.337855
H -0.307478 -1.268041 2.172274
H -0.615889 -2.501350 -0.218453
H 1.017208 -2.419920 0.445724
H -2.541856 0.622482 -0.988336
H -2.097728 -1.040520 -1.365549
H 0.717113 -1.413866 -2.020334
H -0.372063 0.777457 -2.154114
H 0.458514 1.062465 2.046717
H 2.905680 -0.550068 -1.117631
H 2.772292 0.727009 1.101772

***endo*-471**
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C 0.323982 -0.962971 1.180075
C 0.862916 -0.658954 -1.190962
C 0.917705 -1.696896 -0.044570
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H 0.706001 1.041656 2.085623
H -0.745889 0.704348 -1.928861
H 0.659151 -1.403623 2.125420
H 0.859248 -1.137033 -2.176435
H 1.950617 -2.023893 0.121369
H 0.335337 -2.598778 -0.266012
H 3.009325 -0.272656 -1.320667
H 2.006287 1.136444 -1.661861
H 2.883484 0.043016 1.032000
H 2.543013 1.708085 0.575738
H -1.747207 -1.524272 -1.044281
H -1.710117 -0.364882 1.737231
H -1.572942 -2.055929 1.259442
H -2.679694 0.962879 -0.154428

488
C 1.907751 -0.368761 -1.119957
C 0.427851 -0.809808 -1.182717
C 0.216736 -1.802721 -0.017302
C 2.247753 -0.002887 0.355320
C 0.009026 -0.908861 1.231517
C 0.923654 0.358216 1.087770
C -0.489645 0.454910 -0.936337
C 0.232241 1.304517 0.114444
O -2.887096 0.096213 -0.705700
C -1.478204 -0.493805 1.192854
C -1.780770 0.024654 -0.219509
O 0.262695 2.515954 0.143226
H 2.555163 -1.177410 -1.477925
H 2.073919 0.491568 -1.779728
H 0.179825 -1.252278 -2.151829
H 1.084532 -2.464495 0.077198
H -0.657768 -2.445825 -0.172112
H 2.940207 0.843042 0.399812
H 2.729689 -0.841553 0.871212
H 0.247249 -1.436241 2.160796
H 1.109931 0.849329 2.046792
H -0.715501 1.018141 -1.843159
H -2.150467 -1.326533 1.424353
H -1.699928 0.312201 1.907886

544
C -0.591403 1.185098 0.292365
C -0.093849 -0.001765 1.156837
C -0.591175 -1.185896 0.288372
C 0.296688 1.262946 -0.990116
C 0.296135 -1.259066 -0.994776
C 1.176553 0.001920 -1.105445
C 1.420809 -0.002615 1.406598
C 2.189876 -0.000447 0.055183
C -2.052776 -0.780182 -0.020648
C -2.052677 0.780007 -0.018529
H -0.550434 2.136348 0.835719
H -0.627859 -0.003391 2.117109
H -0.549683 -2.138973 0.828489
H -0.333906 1.370806 -1.882586
H 0.941591 2.150752 -0.957319
H -0.334961 -1.362918 -1.887366
H 0.940573 -2.147350 -0.965950
H 1.712180 0.003571 -2.063314
H 1.690993 0.872834 2.010588
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H 2.841120 0.879363 -0.021108
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H -2.401649 -1.202316 -0.969942
H -2.723096 -1.161164 0.758835
H -2.401096 1.204562 -0.966847
H -2.723527 1.158899 0.761602

545
C -0.105436 -0.269220 1.141016
C -0.590823 1.070205 0.552390
C 0.329188 1.468054 -0.631139
C -0.654326 -1.192355 0.023577
C 1.136125 0.236005 -1.089225
C 0.196650 -0.977465 -1.267046
C 2.162759 -0.103688 0.007831
C 1.413699 -0.348097 1.348344
O -1.926039 0.799083 0.085135
C -2.066150 -0.616201 -0.117967
H -0.630222 -0.471846 2.082823
H -0.669453 1.875182 1.290657
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H -2.508678 -0.794493 -1.105993

547
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C -0.547070 -0.489621 -1.350661
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C 0.547493 -0.489520 1.350729
C 1.451949 -0.439055 0.113484
O 2.562343 -0.920466 0.066401
O -2.562333 -0.920473 -0.066929
H -0.776512 2.559031 1.015978
H -1.438022 0.301864 1.923421
H 0.774915 2.559652 -1.015771
H -1.079175 -0.040782 -2.196128
H -0.360557 -1.539314 -1.609926
H 1.437983 0.302978 -1.923277
H 1.079168 -0.040755 2.196499
H 0.361557 -1.539453 1.609453

556
C -1.399056 -1.234638 -0.513008
C 0.085637 -1.222164 -0.230830
C 0.899781 -0.374955 -1.266427
C -1.942734 -0.010971 -0.579859
C 0.132645 0.962924 -1.500199
C -0.987437 1.160548 -0.424881
C 0.408537 -0.420748 1.069763
C -0.317630 0.939124 0.943811
C -2.137693 -2.531149 -0.676595
C 2.216478 -0.149413 -0.541372
C 1.936695 -0.162323 0.956120
O -0.340208 1.752243 1.846713
C 3.409649 -0.011371 -1.119123
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C 0.007476 -1.109185 2.375548
H 0.502168 -2.234166 -0.159381
H 1.044745 -0.898601 -2.215777
H -3.002087 0.170850 -0.749369
H -0.352055 0.954732 -2.482645
H 0.828024 1.809750 -1.484285
H -3.201785 -2.366725 -0.875177
H -2.051705 -3.156279 0.222776
H -1.723553 -3.121208 -1.506013
H 2.231863 0.763367 1.463638
H 2.483918 -0.980802 1.443029
H 4.314804 0.144720 -0.536556
H 3.529049 -0.046992 -2.199554
H -0.939584 3.331895 -0.367927
H -2.439900 2.631084 0.240067
H -2.123018 2.655657 -1.508836
H 0.215612 -0.453100 3.226245
H 0.566764 -2.043105 2.506920
H -1.062958 -1.342941 2.388698

558
C 1.963436 -0.414404 -0.351022
C 1.055720 0.685507 -0.882982
C 0.149064 -0.049703 -1.913766
C 1.276286 -1.437061 0.185369
C -0.905375 -0.766433 -1.045651
C -0.226914 -1.231388 0.328024
C 0.147191 1.240246 0.285921
C -0.174330 0.042114 1.192855
C 3.449181 -0.354253 -0.542399
C -1.944941 0.287661 -0.716146
C -0.963590 -2.383802 0.996229
C 0.787103 2.401835 1.037857
C -1.274567 1.583361 -0.259346
O -0.385832 0.097457 2.386387
C -3.264216 0.107171 -0.792815
H 1.618010 1.505226 -1.343169
H 0.745461 -0.747261 -2.508832
H -0.339003 0.641691 -2.609754
H 1.744067 -2.324644 0.605866
H -1.348233 -1.632802 -1.546204
H 3.941946 -1.255970 -0.164644
H 3.881103 0.512774 -0.024135
H 3.708673 -0.242592 -1.604764
H -2.033458 -2.163661 1.073465
H -0.585068 -2.545671 2.009939

H -0.840961 -3.309699 0.422219
H 0.218447 2.628328 1.944779
H 0.825707 3.301809 0.412344
H 1.810580 2.155588 1.343568
H -1.866688 2.078366 0.517934
H -1.180087 2.293813 -1.093413
H -3.967182 0.891490 -0.520997
H -3.690959 -0.831550 -1.138067

***exo*-559**
C 2.086017 -0.345635 -0.186335
C 1.154510 0.698130 -0.793263
C 0.380161 -0.128664 -1.861350
C 1.417852 -1.395488 0.313166
C -0.697151 -0.872202 -1.035791
C -0.089073 -1.219884 0.407448
C 0.093119 1.245825 0.258628
C -0.185921 0.087085 1.263423
C 3.575010 -0.220971 -0.318192
C -1.818424 0.136740 -0.907451
C -0.805932 -2.406698 1.046538
C 0.602734 2.508497 0.954784
C -1.263290 1.486254 -0.457786
C -3.097701 -0.102048 -1.195843
O -1.454136 0.185149 1.910578
H 1.705461 1.533545 -1.240099
H 1.062197 -0.811407 -2.375937
H -0.091961 0.499234 -2.624916
H 1.901468 -2.276835 0.731017
H -1.036047 -1.793063 -1.520268
H 0.594715 0.051841 2.033883
H 4.089682 -1.100156 0.083989
H 3.951306 0.665004 0.212119
H 3.874821 -0.102997 -1.369466
H -1.882015 -2.223991 1.107490
H -0.440201 -2.587125 2.064375
H -0.637872 -3.318007 0.459418
H -0.086050 2.836593 1.745477
H 0.704127 3.341848 0.248640
H 1.583226 2.338747 1.416818
H -1.967424 1.985152 0.214026
H -1.112014 2.156272 -1.315942
H -3.860763 0.667365 -1.099522
H -3.432244 -1.079794 -1.534703
H -1.398795 0.910943 2.551121

***endo*-559**
C 1.862015 -0.323611 -0.624183
C 0.864727 0.778627 -0.945897
C -0.124201 0.070884 -1.920822
C 1.273413 -1.407155 -0.102311
C -1.048444 -0.736820 -0.982318
C -0.186707 -1.235201 0.278861
C 0.032468 1.232091 0.332900
C -0.163121 -0.017037 1.248140
C 3.307962 -0.191356 -0.998625
C -2.092700 0.264302 -0.528285
C -0.797425 -2.476639 0.925981
C 0.707732 2.397745 1.053238
O 0.841548 -0.221214 2.239139
C -1.420290 1.569579 -0.101607
C -3.408810 0.046062 -0.507495
H 1.344933 1.648058 -1.409555
H 0.425925 -0.568944 -2.615887
H -0.710617 0.775787 -2.520825
H 1.807635 -2.319056 0.153946
H -1.504252 -1.599692 -1.477545
H -1.137539 0.066474 1.752542
H 3.863058 -1.110675 -0.784048
H 3.787332 0.629012 -0.446350
H 3.430083 0.038936 -2.066994
H -1.858745 -2.319077 1.152158
H -0.279518 -2.713273 1.861661
H -0.718904 -3.346030 0.261777
H 0.142545 2.702110 1.945064
H 0.777600 3.275626 0.399642
H 1.720256 2.127330 1.370802
H 0.669069 0.411830 2.952164
H -1.968848 2.036917 0.725995
H -1.416030 2.298286 -0.924355
H -4.111426 0.805855 -0.171117
H -3.834657 -0.898593 -0.837657

562
C 1.241649 1.389441 -0.783561
C -0.227830 1.226198 -0.455999
C -0.914976 0.119066 -1.310903
C 2.041750 0.104740 -0.573049
C 0.024414 -1.129732 -1.351604
C 1.096716 -1.075033 -0.226909
C -0.439437 0.636446 0.972715
C 0.391509 -0.666645 1.073300
O 1.743297 2.429197 -1.162528
C -2.187342 -0.159950 -0.518923
C 1.850023 -2.394510 -0.077375
C -0.096748 1.579561 2.128925
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O 0.460919 -1.301744 2.106870
H -0.736299 2.189583 -0.563533
H -1.140186 0.451120 -2.328447
H 2.781999 0.276788 0.220397
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H 0.550631 -1.172071 -2.314156
H -0.569514 -2.045965 -1.271487
H 1.169119 -3.202527 0.207990
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H 2.336456 -2.667902 -1.020938
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H -0.738187 2.467610 2.101222
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H -3.423105 -0.860822 -2.088509

563
C 1.998775 -0.409607 -0.540262
C 1.044955 0.690125 -0.992825
C 0.045449 -0.033594 -1.931851
C 1.221937 -1.638517 -0.036709
C -0.987764 -0.700553 -0.992647
C -0.240800 -1.224609 0.303531
C 0.271145 1.235195 0.274988
C -0.005523 0.019452 1.173685
O 3.209232 -0.345560 -0.577630
C -1.942115 0.402998 -0.577996
C -1.013872 -2.319396 1.030001
C 1.029306 2.348489 0.989865
C -1.174886 1.650068 -0.143529
C -3.271510 0.296038 -0.574150
O -0.032180 0.041073 2.386344
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H 0.564380 -0.764226 -2.562601
H -0.449440 0.667058 -2.611791
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564
C -1.972446 -0.396497 0.567475
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C 0.000064 0.000004 1.925107
C -1.207238 -1.634906 0.067364
C 1.009492 -0.710187 0.988563
C 0.253320 -1.232886 -0.298401
C -0.253273 1.232929 -0.298377
C -0.000121 0.000000 -1.182679
O -3.180994 -0.330173 0.627979
C 1.972555 0.396545 0.567501
C 1.016998 -2.339200 -1.019683
C -1.016956 2.339291 -1.019573
C 1.207362 1.634894 0.067240
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H 0.508803 0.712813 2.583089
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H 2.055374 -2.041584 -1.201688
H 0.555650 -2.554272 -1.987605
H 1.026934 -3.257305 -0.421495
H -0.555798 2.554220 -1.987617
H -1.026621 3.257443 -0.421453
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567
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C 0.927909 -0.771183 1.024167
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H -2.135036 0.403010 2.074285

569
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C 0.909594 -1.092194 0.808637
C 1.246681 0.188499 -0.085041
C -1.246678 0.188554 0.084922
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C 0.020649 -0.664933 1.960762

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C -2.532690 0.888334 -0.333831
C -1.133608 -0.097744 1.578177
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H -0.268410 -0.895747 -2.993259
H -1.837100 -1.568939 -1.136719
H 0.565291 -2.697300 -0.682233
H -0.565285 -2.696990 0.683452
H 1.899901 0.255781 -2.263038
H 1.837093 -1.568412 1.137427
H 0.268362 -0.894337 2.993652
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291
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C 1.304325 -0.54812 -1.070641
C 3.773392 0.03592 -1.102772
C 2.744548 -1.057051 -0.751728
C 1.961295 -0.15546 1.379342
C 2.83091 -1.280622 0.778422
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C -2.175235 -1.12823 0.500782
C -3.599163 -1.196795 -0.083441
C -1.961296 0.155469 1.379341
C -3.773391 -0.035929 -1.102772
C -2.830909 1.280628 0.778413
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H 1.420667 1.627113 -1.497685
H -1.420667 -1.627124 -1.497674
H 1.959849 2.034749 1.07975
H 0.427645 -2.337923 -0.144187
H -0.232919 1.310476 2.047978
H 0.232918 -1.310461 2.047987
H 3.75637 2.168265 -0.568312
H 4.343429 1.125976 0.719827
H 1.081757 -0.694986 -2.134996
H 4.792127 -0.369049 -1.063396
H 3.614363 0.390629 -2.129303
H 2.946782 -1.981086 -1.306995
H 2.20855 0.040695 2.429915
H 3.873141 -1.229455 1.116345
H 2.451228 -2.263907 1.080103
H -2.946782 1.981076 -1.30701
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H -4.34343 -1.12597 0.719835
H -3.756371 -2.168269 -0.568296
H -2.20855 -0.040678 2.429916
H -4.792126 0.369041 -1.063401
H -3.614362 -0.390646 -2.129301
H -3.873141 1.229465 1.116336
H -2.451226 2.263915 1.080087

Calculated isotropic shieldings and resulting computational shifts
1C 151.8746 36.61172807
2C 153.6525 34.76647639
3C 151.8197 36.66870784
4C 151.8200 36.66839647
5C 156.472 31.84016606
6C 153.625 34.79501816
7C 150.8872 37.63653347
8C 150.8872 37.63653347
9C 165.9373 22.01629476
10C 151.8749 36.61141671
11C 163.51 24.53554748
12C 158.1559 30.09247535
13C 153.6784 34.73959523
14C 162.5934 25.48687078
15C 158.1561 30.09226777
16C 156.4725 31.83964712
17C 165.9366 22.01702128
18C 153.6788 34.73918007
19C 163.51 24.53554748
20C 162.5913 25.48905034
21H 30.0392 1.605451006
22H 29.9165 1.719199036
23H 29.9967 1.644850283
24H 29.9967 1.644850283
25H 30.1753 1.479280616
26H 29.9165 1.719199036
27H 29.9503 1.687865023
28H 29.9503 1.687865023
29H 30.1347 1.516918513
30H 29.8328 1.796792435
31H 30.0392 1.605451006
32H 30.1514 1.501436915
33H 30.0644 1.582089552
34H 29.9914 1.649763604
35H 29.9532 1.685176601
36H 30.2918 1.371280245
37H 30.234 1.424863261
38H 29.9914 1.649763604
39H 30.1752 1.47937332
40H 29.8332 1.796421619
41H 30.1345 1.517103921
42H 29.9531 1.685269306
43H 30.1515 1.501344211
44H 30.0643 1.582182256
45H 30.2925 1.370631315
46H 30.2337 1.425141374

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C -2.397202 -1.092086 -0.40671
C -0.066683 0.781242 -0.934933
C -3.390441 -0.956923 0.766776
C -1.502743 1.181135 -0.518039
C -0.733969 -0.248205 1.321999
C -1.69739 0.914648 1.022001
C -4.818128 -1.180729 0.232348
C -2.541597 0.261111 -1.19265
C -5.006123 -0.324964 -1.051841
C -3.983155 0.827326 -1.003019
C -3.177431 0.511166 1.281094
C -4.060112 1.437735 0.418367
C 1.502742 -1.181145 -0.518012
C 0.951414 1.239804 0.124948
C 4.81813 1.180734 0.232319
C 2.397202 1.092077 -0.406733
C 0.733966 0.248236 1.321994
C 2.541598 -0.261138 -1.192642
C 1.697388 -0.914623 1.022023
C 3.390442 0.956941 0.766753
C 3.983156 -0.827352 -1.002993
C 3.177429 -0.511135 1.281108
C 5.006129 0.324932 -1.051843
C 4.060111 -1.437725 0.418407
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H -0.773744 -2.279483 0.42895
H -2.647876 -1.951395 -1.042049
H 0.164666 1.203294 -1.92145
H -3.165165 -1.681867 1.558749
H -1.674677 2.235595 -0.766959
H -0.963688 -0.724424 2.2838
H -1.450462 1.805178 1.614225
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H -2.32757 0.12796 -2.260585
H -6.027559 0.070526 -1.111769
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H -4.19627 1.575763 -1.776032
H -3.414485 0.592963 2.349032
H -5.099307 1.46998 0.767933
H -3.685875 2.467685 0.452771
H 1.674675 -2.23561 -0.766907
H 0.773743 2.279494 0.4289
H 5.557103 0.906501 0.995783
H 4.97312 2.245325 0.017644
H 2.647876 1.951371 -1.042093
H 0.963683 0.724476 2.283785
H 2.327574 -0.128011 -2.26058
H 1.450458 -1.80514 1.614266
H 3.165168 1.681905 1.558709
H 4.19627 -1.57581 -1.775987
H 3.414481 -0.592904 2.349048
H 6.027563 -0.070565 -1.111754
H 4.849417 0.932387 -1.952518
H 5.099306 -1.46996 0.767976
H 3.685875 -2.467675 0.452838

Calculated isotropic shieldings and resulting computational shifts
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2C 152.54 35.92112091
3C 151.3453 37.1610794
4C 153.9124 34.49673067
5C 156.8371 31.46123508
6C 154.0892 34.313233
7C 152.0352 36.44504411
8C 150.6398 37.89330566
9C 165.5459 22.42252206
10C 150.8427 37.68271925
11C 163.732 24.30513752
12C 158.2453 29.99968864
13C 153.96 34.44732745
14C 162.678 25.39906591
15C 154.089 34.31344058
16C 152.5389 35.92226258
17C 165.5461 22.42231448
18C 151.3454 37.16097561
19C 152.0337 36.44660093
20C 150.8425 37.68292683
21C 150.6405 37.89257914
22C 156.8361 31.46227296
23C 158.2454 29.99958485
24C 153.9602 34.44711988
25C 163.732 24.30513752
26C 162.678 25.39906591
27H 29.8531 1.777973487
28H 29.9612 1.677760267
29H 29.9943 1.647075183
30H 29.8531 1.777973487
31H 30.1724 1.481969037
32H 29.7998 1.827384815
33H 29.8757 1.757022342
34H 30.0421 1.602762585
35H 30.1646 1.489199963
36H 29.9028 1.731899509
37H 30.058 1.58802262
38H 30.0992 1.549828497
39H 29.9646 1.674608325
40H 30.0309 1.613145453
41H 30.0037 1.63836099

42H 30.309 1.355335126
43H 30.2117 1.445536294
44H 29.7998 1.827384815
45H 29.9615 1.677482154
46H 29.9028 1.731899509
47H 30.1646 1.489199963
48H 29.9942 1.647167887
49H 29.8762 1.756558821
50H 30.058 1.58802262
51H 30.0419 1.602947993
52H 30.1727 1.481690924
53H 30.0308 1.613238157
54H 30.0037 1.63836099
55H 30.0993 1.549735793
56H 29.9646 1.674608325
57H 30.309 1.355335126
58H 30.2116 1.445628998

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C -4.604995 -0.727717 0.993391
C -2.739998 1.013467 -0.816881
C -1.948683 0.112809 1.323537
C -2.921867 1.153538 0.741359
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C -6.238923 -0.591249 -0.911487
C -5.222035 0.537668 -1.171948
C -4.396873 0.825081 1.109091
C -5.291801 1.494386 0.044279
C 0.283308 -1.251687 -0.231837
C -0.283308 1.251687 -0.231838
C 3.619325 1.156996 -0.113114
C 1.160614 0.983638 -0.72475
C -0.484761 0.598602 1.181225
C 1.304155 -0.525444 -1.128466
C 0.484761 -0.598602 1.181225
C 2.168402 1.156142 0.426336
C 6.035016 1.086627 0.547731
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C 1.948683 -0.112808 1.323537
C 3.77874 0.053636 -1.221073
C 2.921867 -1.153537 0.741359
C 4.604995 0.727718 0.993391
C 5.222035 -0.537669 -1.171947
C 4.396873 -0.825081 1.109092
C 5.291801 -1.494386 0.044279
C 6.238923 0.591249 -0.911487
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H -1.983071 -2.080683 0.988127
H -3.86829 -2.152697 -0.502389
H -1.083987 0.678316 -2.192797
H -4.36982 -1.222179 1.943932
H -2.919889 1.966815 -1.328876
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H -2.676361 2.168076 1.081079
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H -3.572772 -0.457626 -2.220252
H -7.26298 -0.227644 -1.061443
H -6.087382 -1.410141 -1.626625
H -5.44457 1.060064 -2.110375
H -4.626112 1.178789 2.121875
H -6.3285 1.611005 0.382881
H -4.923918 2.50015 -0.191366
H 0.471782 -2.332569 -0.203777
H -0.471782 2.332569 -0.203778
H 3.86829 2.152697 -0.50239
H 1.394867 1.647851 -1.566665
H -0.247579 1.305975 1.986242
H 1.083987 -0.678317 -2.192797
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H 1.983071 2.080683 0.988126
H 6.769246 0.628053 1.222144
H 6.18526 2.171216 0.615981
H 2.919889 -1.966816 -1.328875
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H 3.572772 0.457625 -2.220252
H 2.676361 -2.168076 1.08108
H 4.36982 1.222179 1.943932
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H 6.3285 -1.611005 0.382881
H 4.923918 -2.50015 -0.191366
H 7.26298 0.227644 -1.061443
H 6.087382 1.410141 -1.626625

Calculated isotropic shieldings and resulting computational shifts
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3C 151.4978 37.00280228
4C 152.5457 35.91520498
5C 156.3892 31.92610275
6C 155.3201 33.03570317
7C 154.051 34.35288012
8C 148.825 39.77685522
9C 165.8604 22.09610794
10C 149.2722 39.31271406
11C 163.7255 24.31188376
12C 159.4054 28.79564089
13C 155.0133 33.35412558
14C 162.7794 25.2938246
15C 153.8961 34.51364816
16C 153.8949 34.51489362
17C 151.4981 37.00249092
18C 154.1436 34.25677218
19C 153.0039 35.43964712
20C 152.5451 35.91582771
21C 153.005 35.43850545
22C 151.7733 36.71686559
23C 165.8606 22.09590036
24C 155.3198 33.03601453
25C 154.05 34.35391801
26C 149.2718 39.31312922
27C 148.8252 39.77664764
28C 156.3893 31.92599896
29C 159.4054 28.79564089
30C 155.0135 33.35391801
31C 162.7793 25.29392839
32C 163.7255 24.31188376
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42H 29.9978 1.643830537
43H 30.1749 1.479651432
44H 30.1807 1.47427459
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47H 30.1432 1.509038658
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49H 30.2322 1.426531937
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53H 29.748 1.875405581
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63H 29.9924 1.648836563
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65H 29.8792 1.753777695
66H 30.1432 1.509038658
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68H 30.2323 1.426439232
69H 30.1807 1.47427459
70H 30.0796 1.567998517

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C -6.84907 1.261561 0.579862
C -5.381185 1.372423 0.076409
C -7.038884 -0.143948 1.254313
C -6.059101 -1.061219 0.493633
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C -6.241357 -0.655714 -1.013319
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C -4.604332 -0.783614 0.942733
C -3.607575 -1.201027 -0.15314
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C -3.772429 -0.094088 -1.253338
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C -1.151253 -0.994647 -0.760394
C -0.295119 1.249011 -0.267151
C -1.309352 0.514215 -1.163653
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C 2.934164 -1.124051 0.702133
C 4.390966 -0.765162 1.086197
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H -0.493219 2.328188 -0.238538
H -1.090864 0.668955 -2.228026
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H 1.09083 -0.669325 -2.227951
H 1.958827 2.101818 0.953248
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H 2.699644 -2.140199 1.044668
H 4.598892 -1.10531 2.108834
H 2.948931 -1.936971 -1.36337
H 3.563313 0.490035 -2.255396
H 4.404236 1.304672 1.887739
H 3.841018 2.197496 -0.549726
H 5.144551 -2.422797 -0.13649
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H 5.406382 -1.048338 -2.123107
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H 7.929586 0.140909 -2.314573
H 9.721996 0.747791 -0.739434
H 8.537332 2.047916 -0.659023
H 8.604639 1.59449 1.666961
H 9.202812 -0.041971 1.434355

Calculated isotropic shieldings and resulting computational shifts
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2C 166.5631 21.36678775
3C 160.0958 28.07908666
4C 164.3246 23.69008822
5C 155.387 32.96626881
6C 149.7703 38.79574468
7C 157.1863 31.09880643
8C 152.2175 36.25583809
9C 154.7221 33.65635703
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11C 155.644 32.69953295
12C 151.4394 37.06341463
13C 151.759 36.73170732
14C 154.2863 34.10866632
15C 154.9371 33.43321225
16C 151.5882 36.90897769
17C 153.6475 34.7716658
18C 152.72 35.73430202
19C 151.4363 37.06663207
20C 153.4615 34.96471199
21C 153.287 35.14582252
22C 152.2311 36.24172289
23C 152.7164 35.7380384
24C 153.6482 34.77093928
25C 153.2905 35.14218993
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28C 153.4621 34.96408926
29C 151.4387 37.06414115
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32C 151.5885 36.90866632
33C 151.761 36.72963155
34C 154.2838 34.11126103
35C 149.7738 38.79211209
36C 155.3872 32.96606124
37C 154.7202 33.65832901
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39C 157.1871 31.09797613
40C 152.2177 36.25563051
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42C 160.0954 28.07950182
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92H 30.1491 1.503569111
93H 30.3288 1.336979698
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C -7.433796 -0.726416 1.086566
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C -3.181223 1.253855 -0.357564
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C -2.348765 -0.443446 1.20251
C -0.897883 0.092585 1.282407
C -2.545106 -1.223965 -0.145858
C -1.552859 -0.552603 -1.114263
C -0.723017 1.286398 0.278244
C -1.735288 0.982739 -0.842699
C 0.099578 -0.968231 0.778791
C 1.55286 -0.552599 1.114265
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C 0.897884 0.09258 -1.282407
C 1.735289 0.982742 0.842696
C 0.723018 1.286397 -0.278248
C 2.545106 -1.223965 0.145862
C 4.000094 -1.037892 0.644304
C 2.348766 -0.44345 -1.202508
C 3.351835 0.722097 -1.108873
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C 3.181223 1.253856 0.357561
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C 8.107734 0.326865 1.172087
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C 9.09058 -0.801852 0.801274
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Calculated isotropic shieldings and resulting computational shifts
1C 165.071 22.91541256
2C 166.2806 21.65998962
3C 160.3352 27.83061754
4C 164.4560 23.55371043
5C 155.634 32.70991178
6C 149.013 39.58173326
7C 156.9361 31.35848469
8C 152.441 36.0238713
9C 157.1945 31.0902958
10C 148.1068 40.52226258
11C 155.0178 33.34945511
12C 153.4239 35.00373638
13C 151.7836 36.7061754
14C 154.8608 33.5124027
15C 153.7934 34.62023871
16C 152.5318 35.92963155
17C 153.2368 35.19792423
18C 152.4831 35.98017644
19C 153.4854 34.93990659
20C 152.7778 35.6743124
21C 152.0766 36.40207577
22C 152.4307 36.03456149
23C 152.5279 35.93367929
24C 152.7793 35.67275558
25C 152.5296 35.93191489
26C 152.4814 35.98194084
27C 152.428 36.03736378
28C 152.0778 36.40083031
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30C 154.8592 33.51406331
31C 153.2383 35.19636741
32C 153.4235 35.00415153
33C 152.5328 35.92859367
34C 153.7935 34.62013492
35C 151.7846 36.70513752
36C 152.441 36.0238713
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38C 149.0139 39.58079917
39C 148.1079 40.52112091
40C 157.194 31.09081474
41C 156.9377 31.35682408
42C 155.6342 32.7097042
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46C 164.4549 23.5548521
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98H 30.1236 1.527208677

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